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Comparative Study of Inflammatory Cytokine Levels and Thrombocytopenia during Plasmodium Falciparum and P. Vivax Infections

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Abstract – The most commonly observed complication of malaria infections is trombocytopenia. The point of this study was to understand the possible relationship between P. vivax, P. falciparum's notorious cytokines and blended infections across various degrees of thrombocytopenia. A hospital-based cross-sectional study was performed in India. In this study, blood samples from 627 patients with Maalria fever were examined for contaminated parasite species, clinical conditions, platelet levels and key cytokines produced in response to disease; samples from 176 uninfected solid people were utilized as controls. Approximately 62.7% of patients had gentle to direct levels of thrombocytopenia and 16% had serious thrombocytopenia (platelets<50?? 103/µl). In general, the consequences of our study propose that infammatory cytokines impact the change of mellow types of thrombocytopenia into extreme structures during malarial infections. Further investigations are expected to understand the relationship of infammatory cytokine responses with extreme intestinal sickness complications and thrombocytopenia.

Keywords: Thrombocytopenia, Inflammatory Cytokine Levels, Plasmodium falciparum, P. vivax,

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INTRODUCTION

In many regions of India, malaria continues to be endemic. In the form of anaemia, leucopenia, and thrombocytopenia, haematological alterations are prevalent in malaria.1 Deep thrombocytopenia is common in Plasmodium falciparum malaria1-3 but rare with only a few case reports in Plasmodium vivax malaria.4, 5 in a 7-year-old male child, we report on this rare presentation.

With as many as 500 million cases annually, malaria remains a major cause of mortality in the tropical world. Severe malaria is a multi-system disorder that has multiple manifestations, requires hospitalisation, parenteral antimalarial therapy, and adequate management of evolving complications. Malaria plasmodia, primarily inside their host-cell erythrocytes, spend the majority of their complex life cycle intracellularly, providing an extraordinary example of parasitism. In light of this relationship among parasites and red cells, there are various ramifications for the blood of the host that reach out a long ways past the immediate impact of parasitized red platelets, including extreme pallor, coagulation issues, mathematical or useful leukocyte changes and spleen contribution.

Plasmodium vivax is the most widespread parasite of human malaria, placing 3.3 59 billion people globally at risk (1). More recently, the burden of P. vivax (Pv) 60 has been aggravated by increasing evidence of its presence across all African regions (2). 61 Its capacity to relapse, its 62 outstanding transmission effectiveness and low-thickness blood-stage infections, often 63 undetected by routine reconnaissance, remember troubles for controlling and taking out Pv. (3).

A common clinical complication for Pv malaria is plasmodium vivax-induced severe thrombocytopenia (PvST), characterised by blood platelet counts below 50,000 per mm3. The mechanisms that contribute to PvST are unclear, but may be associated with platelet activation, intake and/or phagocytosis (4, 5)

Given the multifactorial mechanisms through which platelets can affect Pv 91 malaria, crucial factors and pathways that might underlie a PvST fingerprint have been investigated here. To this end, in a cohort of P. vivax patients with varying degrees of thrombocytopenia, we measured the plasma concentrations of cytokines, chemokines and growth factors. We included a group of microRNAs (miRNAs), a class of small non-96 coding RNAs that regulate gene expression and

appear to be critical for regulating platelet function, to gain additional insights into potentially disturbed regulatory pathways in PvST (6, 7). We offer essential insights into the interaction between inflammatory mediators, miRNAs, and P. vivax-induced severe thrombocytopenia by combining these highly sensitive methods with machine learning algorithms.

METHODOLOGY

Between November 2013 and October 2015, a prospective hospital-based study was conducted at the hospital. A total of 803 individuals were randomly recruited into the study between the ages of 15 and 65. In the wake of getting educated assent from the study, all participants were orally educated about the study and selected pa All contaminated patients had regular malarial symptoms, for example, irregular fever , chills, and afflictions and were treated in the outpatient and inpatient departments of District Wenlock Hospital in Mangaluru as solid controls (HC). Those going to the blood donation center for blood gifts and negative malaria testing.

Mindful microscopic assessment of peripheral blood spreads recolored by Giemsa has affirmed malarial infections. Two good and bad blood slides, recolored with 4% Giemsa stain and saw under the microscope for the presence of Plasmodium and the recognizable proof of the type of parasite species were prepared from every participant in the study. Blood parasite densities were resolved as parasites/µl of blood (number of parasites tallied/number of white platelets, WBCs checked?? all out number of WBCs per µl of blood) or (number of parasites checked/number of red platelets RBCs tallied?? absolute number of RBCs per µl of blood) As a percentage of parasitemia, the quantity of parasites per µl blood/number of RBCs per µl blood per 100 was resolved. There were no PCR investigations directed for malarial determination.

Before any antimalarial drug was controlled, approximately 2-3 ml of venous blood was aseptically brought into sterile heparin-covered vacuum tubes for plasma preparation and into clump activator tubes for serum preparation and kept up at 4 C. After centrifugation, serum and plasma samples were prepared, named and put away at −70?? C until additional utilization. The contaminated patients were treated as per the National Vector Borne Disease Control Program [NVBDCP] suggestions. (8). Patients infected with Te P. vivax were treated with a combination of chloroquine for 3 days and primaquine for 14 days, and patients infected with P. falciparum were treated with a single dose of artemisinin-based combination therapy (artesunate plus sulfadoxine-pyrimethamine) and primaquine. Patients with severe complications of malaria who required supportive treatment were admitted to the hospital and treated by the attending physician.

Platelet check, mean platelet volume (MPV), plateletcrit (PCT), and platelet conveyance width (PDW) were dictated by utilizing a computerized hematology analyzer (Mind RayBiomedical, Shenzhen, China). The sandwich ELISA duplicate examination of cytokines, TNF-µ, IL-6, and IL-10 in plasma was performed utilizing R&D Biotech, USA, units, as taught by the producer. The plasma examination of cytokines, TNF-µ, IL-6, and IL-10 was performed in duplicate by sandwich ELISA utilizing R&D Biotech, USA units, as trained by the producer.

Study Participants

Study participants were grouped into I HC, patients who tried negative for Plasmodium parasite presence, (ii) uncomplicated malaria (UM), patients with poor quality fever, cerebral pain or chills and who were positive for Plasmodium parasite peripheral blood smear (these patients were dealt with outpatiently) and (iii) severe malaria (SM), patients requiring hospital ad hospital ad Trombocytopenia is defined as a decrease of 150 ⁇ 103 /µl in platelet counts, (ii) mild thrombocytopenia (MT, 100-150 ⁇ 103 /µl), (iii) moderate thrombocytopenia (MDT, 50-100 ⁇ 103 /µl), and (iv) severe thrombocytopenia (ST, < 50 ⁇ 103 /µl).

Statistical Analysis

Graphpad Prism version-6 (Graphpad Prism software Inc., San Diego, CA, USA) and R version 3.4.2 (https:/www.r-project.org/) were used to perform the statistical analysis. The mean ± standard deviation and mean ± interquartile range are presented as quantitative variables. Rundown measurements were utilized for standard demographics and quantitative factors. The Kruskal-Wallis Test conducted a comparison of nonparametric data between different groups and the significance between two groups was determined by the Mann-Whitney U Test with a 95 percent confidence interval with multiple testing adjustments. For the determination of correlations between two continuous variables, Spearman rank correlation was used. To decide the equity of proportions or percentages, a three-sample test without congruity amendment. If significant, a two-sample binomial proportion test was used to obtain the highest significant proportion. It was considered that P values below 0.05 were significant.

RESULTS

Demographics of Study Participants:

An aggregate of 800 and three (n=803) people comprising 627 (78.1 percent) malarial contaminated patients and 176 (21.9 percent) as HC were tried out the study at Government Wenlock Hospital in Mangaluru City. So, the study participants' mean age (counting HC) was 30.3

years (age range, 16 to 65 years). The majority of people infected were men (402, 64.1 percent) and the number of women was 225 (35.9 percent). Among the 627 patients tainted, 554 (88.4 percent) had MM and were treated on an outpatient premise, and 73 (11.6 percent) patients required confirmation because of SM complications. Pv was the most prevalent infection species (n=384, 61.3 percent) among the different infecting species, followed by Pf (n=172, 27.4 percent) and mixed (n=71, 11.3 percent) infections (Table 1).

Table 1: Characteristics of study participants across various infecting species

	Healthy controls	*P. vivax*	*P. falciparum*	Mixed	Overall Infected	p value[a]
Number of study participants, n (%)	176	384(61.3)	172 (27.4)	71 (11.3)	627 (100)	<0.0001
Uncomplicated malaria (UM)	0	351 (63.4)	149 (26.9)	54 (9.7)	554 (88.4)	<0.0001
Severe malaria (SM)	0	33 (45.2)	23 (31.5)	17 (23.3)	73 (11.6)	0.6853
Gender, n (%)						
Males	116	246 (61.2)	111(27.6)	45 (11.2)	402(64.1)	0.9866
Females	60	138 (61.3)	61 (27.1)	26(11.6)	225 (35.9)	0.9866
Age (in years, mean, range)	30.1 (16-58)	30.5 (16-65)	32.7 (16-65)	31.7 (16-65)	30.3 (16-65)	>0.05

Data represented p values as the number of study participants (percentages) when three infecting groups were compared from the multinomial proportion test.

Platelets and Infammatory Cytokines Profle of the Study Participants:

RBC, hemoglobin, platelets, platelet files and plasma levels of infammatory cytokines were compared between I HC and tainting groups, and (ii) between various groups of infectors. Mean parasitemia was higher in patients with P. falciparum(0.8±1.15 percent) than in the blended (0.6±0.75 percent) and P. vivax (0.3±0.49 percent) groups, showing a higher parasitic weight during Pf contamination (Table 2). A huge decline in RBC tallies over all contaminating species was seen in comparison with HC (p<0.0001); Pf disease brought about essentially diminished RBC checks inside the diverse tainting species. A noteworthy negative connection was seen between the levels of RBC and parasitic weight during Pf (r=-0.0218, p=0.0076) and Pv (r=-0.1322, p=0.0104) disease. Hemoglobin levels among various tainting species were altogether diminished compared to HC (p<0.0001), and hemoglobin levels among Pf patients among different contaminating species were essentially decreased (p<0.0001) (Table 2). A significant negative correlation was observed between increased parasitemia and decreased levels of haemoglobin in all patients, irrespective of the infected parasite species; Pv (r=-0.3145, p<0.0001), particularly during infections with Pf (Table 2). Platelet levels were reduced in all three infected groups as parasitemia increased during infections with Pv (r=-0.2140, p=0.0003), Pf (r=-0.1929, p=0.0169) and mixed infections (Pv and Pf) (r=-0.1170, p=0.0053). Infammatory cytokine plasma levels of Te were significantly increased by malarial infections. Compared to HC, the te-levels of TNF-μ, IL6, and IL-10 were significantly increased (p0.05).

Table 2: During malarial disease, changes in hematological parameters and infammatory cytokines

Parameter	Normal range	Healthy controls	*P. vivax*	*P. falciparum*	Mixed	P value[a] (between groups)		
						Pv Vs *Pf*	*Pv* Vs Mixed	*Pf Vs Mixed*
Parasitemia (%)			0.3 ± 0.49	0.8 ± 1.15	0.6±0.75	< 0.001	< 0.0001	0.5957
RBC	4.0-6.0 X $10^3/\mu l$	5.0 ± 0.73	4.7 ±0.92	3.7 ± 0.91	4.8 ±1.98	0.0011	0.5994	0.0485
Hemoglobin	Males: 14-18; Females: 12-16 g/dl	12.5 ± 1.26	11.5 ± 2.86	10.1 ± 2.93	10.7 ±3.22	0.0003	0.0699	0.0383
Platelets	100 - 400 x$10^3/\mu l$	210 ± 57.2	108.2 ± 55.3	92 ± 45.1	101 ±75.3	0.0095	0.7869	0.036
MPV	6.5-12.0 fL	9.4 ± 1.03	10.3 ± 1.63	10.2 ±1.36	10.5 ±1.56	0.7358	0.0216	0.0218
PDW	9.0 - 17.0 %	14.7 ± 3.79	14.9 ± 0.89	14.7 ±1.23	15.0 ±1.19	0.6861	0.479	0.3722
PCT	0.108 - 0.282 %	0.2±0.06	0.1±0.05	0.1±0.05	0.1±0.06	0.9063	0.1112	0.1761
TNF-α (pg/ml)		67.0±29.5	251.8±101.2	259.9±144.0	236.7±190.2	0.1402	0.2536	0.8992
IL-6 (pg/ml)		88.1±54.8	227.4±63.9	280.2±44.4	292.9±94.2	0.0013	0.0038	0.7219
IL-10 (pg/ml)		136.0±66.2	634.9±83.1	671.2±68.6	688.4±43.2	0.6299	0.1061	0.3904

IL-10 is an enemy of infammatory cytokine known to hinder the response of T1 and is produced primarily by macrophages (9). In solid volunteers, organization of human recombinant IL-10 prompts decreased platelet levels. The reduction in Tis is because of diminished production of monocyte and macrophage proinfammatory cytokines, which thusly prompts diminished hematopoietic progenitor cells, for example, province framing megakaryocyte units (CFU-MKs), which thus influence platelet production (10).

Classifcation of Trombocytopenia Intensity among Study Participants:

Among the 176 HCs remembered for this study , most of 168 (95.5 percent) were non-thrombocytopenic (NT), while 6 (3.4 percent) had mellow thrombocytopenia (MT) and 2 (1.1 percent) had moderate thrombocytopenia (MDT). Of the all out 627 patients contaminated, 493 (78.6%) had fluctuating levels of thrombocytopenia; 134 (21.4%) had NT, 188 (30%) had MT, 205 (32.7%) had MDT, and 100 (15.9%) had extreme thrombocytopenia (ST) (Table 3).

Generally, in this endemic setting, just 21.4 percent of patients were non-thrombocytopenic, while 30 % of patients had mellow thrombocytopenia, 32.7% had moderate thrombocytopenia, and 15.9% had extreme thrombocytopenia. Notwithstanding the contaminated parasite species, thrombocytopenia was regularly recognized: Pv (80.5 percent), Pf (79.1 percent), and blended infections (67.6 percent). These outcomes are comparable to previously published perceptions of PV endemic settings (11). The high prevalence of thrombocytopenia might be a potential marker of malarial infections, despite the fact that it isn't possible to recognize thrombocytopenia per se from the contaminating parasite species (12-14).

Table 3: Stratifcation of study participants according to the varying intensity of thrombocytopenia

Thrombocytopenia intensity	Healthy controls	*P. vivax*	*P. falciparum*	Mixed	Overall Infected	p value[a]
Non-thrombocytopenia –NT (platelet levels >150 x10^3/μl)	168 (95.5)	75 (19.5)	36 (20.9)	23 (32.4)	134(21.4)	0.065
Mild thrombocytopenia – MT (platelet levels 100-150x10^3/μl)	6 (3.4)	127 (33.1)	48 (27.9)	13 (18.3)	188 (30)	0.055
Moderate thrombocytopenia –MDT (platelet level 50-100x10^3/μl)	2 (1.1)	129 (33.6)	57 (33.1)	19 (26.8)	205 (32.7)	0.512
Severe thrombocytopenia –ST (platelet levels <50x10^3/μl)	0(0)	53 (13.8)	31 (18.1)	16 (22.5)	100 (15.9)	0.279

Comparison of Cytokine Levels across Varying Degrees of Trombocytopenia:

Among the 176 HCs remembered for this study, most of 168 (95.5 percent) were non-thrombocytopenic (NT), while 6 (3.4 percent) had gentle thrombocytopenia (MT) and 2 (1.1 percent) had moderate thrombocytopenia (MDT). Of the absolute 627 patients tainted, 493 (78.6%) had differing levels of thrombocytopenia; 134 (21.4%) had NT, 188 (30%) had MT, 205 (32.7%) had MDT, and 100 (15.9%) had extreme thrombocytopenia (ST) (Table 3).

By and large, in this endemic setting, just 21.4 percent of patients were non-thrombocytopenic, while 30 % of patients had gentle thrombocytopenia, 32.7% had moderate thrombocytopenia, and 15.9% had serious thrombocytopenia. Despite the tainted parasite species, thrombocytopenia was oftentimes recognized: Pv (80.5 percent), Pf (79.1 percent), and blended infections (67.6 percent). These outcomes are comparable to previously published Pv endemic settings. Mean levels of platelets and plasma cytokines were compared and broke down for various degrees of thrombocytopenia during Pv, Pf, and blended infections (Table 4). Compared to NT groups with expanded thrombocytopenia power during Pv, Pf, and blended infections, TNF-μ levels were discovered to be continuously expanded ($p<0.05$). In patients with Pf infections among ST groups of various tainting species, TNF-μ levels were discovered to be essentially expanded (P-esteem = 0.0032). Te IL-6 levels in ST patients during Pv and Pf infections were discovered to be diminished compared with the NT groups. When compared inside the ST groups across tainting species, the IL-6 levels were essentially lower in Pv patients (esteem = 0.0023). There was likewise a huge diminishing in the IL6/IL-10 proportion, irrespective of the tainting species, with an expansion in thrombocytopenic force, especially during extreme thrombocytopenia.

Compared to the NT groups, levels of IL-10 were discovered to be essentially raised across various forces of thrombocytopenia during Pv, Pf, and blended infections. Nonetheless, the IL-10 levels didn't show any huge change across various tainting species inside the ST groups (Table 4, P-esteem = 0.8379) (11). The high prevalence of thrombocytopenia might be a potential marker of malarial infections, in spite of the fact that it isn't possible to recognize thrombocytopenia from the contaminating parasite species per se (12-14).

Table 4: Cytokines during varying thrombocytopenia levels during patients with P. vivax, P. falciparum, and mixed infections

Cytokines	*P. vivax*			
	NT	MT	MDT	ST
n (%)	75 (19.5%)	127 (33.1%)	129 (33.6%)	53 (13.8%)
Platelets x10^3/μl	183 (162-203)	124 (112-134)	79 (67-90)	30(22-40)
TNF-α (pg/ml)	131.7 (70.6-220.7)	208.0 (108.1-312.0)	213.0 (106.0-362.8)	431.9 (232.4-607.6)
IL-6 (pg/ml)	208.3 (109.0-366.6)	264.0 (154.3-402.4)	173.7 (111.8-249.8)	111.2 (79.9-158.5)
IL-10 (pg/ml)	373.9 (256.1-493.4)	502.1 (352.7-671.4)	641.8 (441.6-892.3)	892.8 (545.5-1556.0)
Cytokines	*P. falciparum*			
n (%)	36 (20.9%)	48 (27.9%)	57 (33.1%)	31 (18.0%)
Platelets x10^3/μl	166 (159-191)	127 (116-135)	80 (68-92)	29 (13-38)
TNF-α (pg/ml)	82.0 (51.0-127.2)	151.8 (56.2-249.5)	193 (78.2-312.5)	602.2 (359.4-761.6)
IL-6 (pg/ml)	247.0 (136.0-370.7)	324.1 (160.2-424.4)	284 (151.8-456.1)	140.4 (116.6-165.6)
IL-10 (pg/ml)	429.7 (169.7-701.5)	486.4 (267.0-751.0)	679.8 (372.2-978.9)	874.9 (348.5-1585.5)
Cytokines	Mixed			
n (%)	23 (32.4%)	13 (18.3%)	19 (26.8%)	16 (22.5%)
Platelets x10^3/μl	162 (154-182)	118 (118-136)	76 (56-84)	29 (20-36)
TNF-α (pg/ml)	83.8 (67.0-160.4)	154.2 (135.3-371.6)	189.1 (107.6-339.0)	284.9 (185.7-473.3)
IL-6 (pg/ml)	237.0 (93.1-308.5)	325.1 (227.3-403.9)	270.5 (153.5-417.7)	241.6 (115.6-380.7)
IL-10 (pg/ml)	506.4 (298.7-729.6)	531.3 (263.7-639.4)	722.1 (509.6-813.5)	883.6 (591.5-1064.1)

Clinical Manifestations in Patients with Malarial Trombocytopenia:

Of the 176 HC, 168 (95.5 percent) were NT and8 (4.5 percent) had levels of gentle to direct thrombocytopenia. Of 627 malaria patients, 493 patients (78.6 percent) had thrombocytopenia. 63 (12.7%) of these thrombocytopenic patients were hospitalized because of serious malarial complications, for example, extreme frailty (17.5%), intense renal disappointment (12.7%), jaundice (27.0%), metabolic acidosis (36.5%), spontaneous dying (3.2%), hypoglycemia (25.4%), hyperparasitemia (4.8%), intense respiratory trouble disorder.

Table 5: Extreme malarial complications for patients with serious thrombocytopenia across various contaminating species

Clinical condition	Total (n=63)	*P. vivax* (n=28)	*P. falciparum* (n=20)	Mixed (n=15)	p value[b]
Severe anemia	11 (17.5)	4 (14.3)	4 (20)	3 (20)	0.499
Acute renal failure	8 (12.7)	4 (14.3)	2 (10)	2 (13.3)	0.063
Jaundice	17 (27.0)	6 (21.4)	5 (25)	6 (40)	0.063
Metabolic acidosis	23 (36.5)	12 (42.9)	8 (40)	3 (20)	0.827
Spontaneous bleeding	2 (3.2)	0 (0)	0 (0)	2 (13.3)	NA
Hypoglycemia	16 (25.4)	7 (25)	6 (30)	3 (20)	0.134
Hyperparasitemia	3 (4.8)	0 (0)	3 (15)	0 (0)	NA
Acute respiratory distress syndrome (ARDS)	1 (1.6)	1 (3.6)	0 (0)	0 (0)	NA
Pulmonary edema	12 (19)	5 (17.9)	4 (20)	3 (20)	0.498
Cerebral malaria (CM)	1 (1.6)	1 (3.6)	0 (0)	0 (0)	NA

CONCLUSION

Our exploration recommends that Pv infections, as seen in Pf and Pk infections, can likewise bring about a comparable level of extreme thrombocytopenia predictable with the previous fndings. Severe malarial complications such as severe anaemia, acute renal failure, jaundice, metabolic acidosis, spontaneous bleeding, hypoglycemia, hyperparasitemia, acute respiratory distress syndrome, pulmonary edoema, and cerebral malaria were also observed in patients with thrombocytopenia, regardless of the infecting species. The results also suggest that cytokines such as TNF-μ TNF T μ-6 and IL-10 may play a role in the reduction or disruption of platelet production, resulting in malarial thrombocytopenia.

In conclusion, since these lines of studies are scarce in India, studies in other regions are justified in supporting the current pattern of thrombocytopenia during malaria. In order to understand the role of infammatory cytokines and their association with severe malaria complications during malaria thrombocytopenia, particularly during infections with P. vivax, studies are also needed.

REFERENCES

1. Battle KE, Lucas TCD, Nguyen M, et al. (2019) Mapping the global endemicity and clinical burden of Plasmodium vivax, 2000-17: a spatial and temporal modelling study. Lancet; 394(10195): pp. 332-43.

2. Twohig KA, Pfeffer DA, Baird JK, et al. (2019) Growing evidence of Plasmodium vivax across malaria-endemic Africa. PLoS Negl Trop Dis; 13(1):e0007140.

3. Price RN, Commons RJ, Battle KE, Thriemer K, Mendis K. (2018) Plasmodium vivax in the Era of the Shrinking P. falciparum Map. Trends Parasitol; 36(6): pp. 560-70.

4. Lacerda MV, Mourao MP, Coelho HC, Santos JB. (2011) Thrombocytopenia in malaria: who cares? Mem Inst Oswaldo Cruz; 106 Suppl 1: pp. 52-63.

5. Coelho HC, Lopes SC, Pimentel JP, et al. (2013) Thrombocytopenia in Plasmodium vivax malaria is related to platelets phagocytosis. PLoS One; 8(5):e63410.

6. Essien EM, Emagha UT. (2014) Blood platelet: a review of its characteristics and function in acute malaria infection. Afr J Med Med Sci; 43(4): pp. 287-94.

7. Stojkovic S, Nossent AY, Haller P, et al. (2019) MicroRNAs as Regulators and Biomarkers of Platelet Function and Activity in Coronary Artery Disease. Thromb Haemost; 19(10): pp. 1563-72.

8. National Institute of Malaria Research, Guidelines for Malaria Treatment in India, NVBDCP, New Delhi, India, 2014 ed edition, 2014.

9. K. N. Couper, D. G. Blount, and E. M. Riley, (2008) “IL-10: the master regulator of immunity to infection,” Te Journal of Immunology, vol. 180, no. 9, pp. 5771–577.

10. J. A. Sosman, A. Verma, S. Moss et al., (2000) “Interleukin 10- induced thrombocytopenia in normal healthy adult volunteers: Evidence for decreased platelet production,” British Journal of Haematology, vol. 111, no. 1, pp. 104–111.

11. S. Margono, B. Lubis, S. Pasaribu, H. Wijaya, and A. P. Pasaribu, (2016) “Te correlation between platelet count and parasite density in children with malaria infection,” Asian Pacifc Journal of Tropical Disease, vol. 6, no. 3, pp. 199–203.

12. U. M. Jadhav, V. S. Patkar, and N. N. Kadam, (2004) “Trombocytopenia in malaria–correlation with type and severity of malaria,” Journal of Association of Physicians of India, vol. 52, pp. 615–618.

13. S. J. Khan, Y. Abbass, and M. A. Marwat, (2012) “Trombocytopenia as an indicator of malaria in adult population,” Malaria Research and Treatment, vol. 2012, Article ID 405981, 4 pages.

14. M. Kotepui, B. Phunphuech, N. Phiwklam, C. Chupeerach, and S. Duangmano, (2014) “Efect of malarial infection on haematological parameters in population near Tailand-Myanmar border,” Malaria Journal, vol. 13, article 218.

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