Access this article online

Quick Response Code:

Website: www.ijhonline.org

DOI: 10.4103/ijh.ijh_58_20

Impact of malaria co-infection on leukocyte indices of tuberculosis-infected participants at pretreatment, intensive, and continuation phase anti-tuberculosis therapy

Chizoba O. Okeke, Martin O. Ifeanyichukwu, Chisom M. Okeke[1], Sylvester N. Ibekailo[2], Sunday Ogamde[3]

Department of Medical Laboratory Science, Faculty of Health Sciences and Technology, College of Health Sciences, Nnamdi Azikiwe University, Awka, [1]Department of Family Medicine, Nnamdi Azikiwe University Teaching Hospital, Nnewi, [2]Department of Human Physiology, Alex Ekwueme Federal University, Ndufu-Alike, [3]Department of Laboratory, Nigerian Institute of Medical Research, Lagos, Nigeria

Address for correspondence:
Dr. Chizoba O. Okeke, Department of Medical Laboratory Science, Faculty of Health Sciences and Technology, College of Health Sciences, Nnamdi Azikiwe University, Nnewi Campus P.M.B. 5001 Anambra State, Nigeria.
E-mail: oc.okeke@unizik.edu.ng

Submission: 20-11-2020
Revised: 05-01-2021
Accepted: 09-01-2021
Published: 21-06-2021

Abstract:

BACKGROUND: Hematological changes involving all blood cells are some of the most common complications in both tuberculosis (TB) and malaria infection. The changes induced by malaria infection are diverse, and the first line anti-TB treatment regimen which involves two phases may alter these changes in TB participants co-infected with malaria (TB/MP).

OBJECTIVE: In this study, we aimed to ascertain the impact of malaria co-infection on leukocyte indices of TB-infected participants at pre-treatment, intensive and continuation phase therapy.

MATERIALS AND METHODS: In this cross-sectional study, 180 participants were recruited comprising; 60 (35 TB and 25 TB malaria) participants before treatment, sixty (36 TB and 24 TB-Malaria) participants after intensive phase treatment and sixty (27 TB and 33 TB-Malaria) participants after continuation phase therapy. Whole blood was used for the measurement of total (total white blood cell [TWBC]) and differential white cell count, Platelet count, and packed cell volume (PCV).

RESULTS: Before initiation of treatment, TWBC, neutrophil, lymphocyte, platelet count, and neutrophil-lymphocyte ratio were significantly reduced (P = 0.041, 0.022, 0.046, and 0.026, respectively), whereas eosinophil count was significantly increased in TB/Malaria participants compared to TB participants (P = 0.043). There was no significant change in these parameters after intensive phase treatment (P > 0.05). However, after continuation phase treatment, PCV was significantly reduced, while eosinophil was significantly increased in TB/Malaria participants compared with TB participants (P = 0.046 and 0.045, respectively).

CONCLUSION: Malaria co-infection induces the significant reduction in leukocyte indices of TB patients at pretreatment but not at the intensive and continuation phase anti-TB therapy except eosinophils count which was increased before treatment and continuation phase treatment.

Keywords:

anti-tuberculosis drugs, malaria, tuberculosis, white blood cells

How to cite this article: Okeke CO, Ifeanyichukwu MO, Okeke CM, Ibekailo SN, Ogamde S. Impact of malaria co-infection on leukocyte indices of tuberculosis-infected participants at pretreatment, intensive, and continuation phase anti-tuberculosis therapy. Iraqi J Hematol 2021;10:48-54.

Introduction

Globally, malaria infection is a major health challenge with about 219 million cases worldwide of which about 92% of the total infection is in Africa.[1] Similar to the global report for malaria infection, Africa with a TB incidence of 237 per 100,000 population has the highest incidence and 25% of incident cases globally.[2] Because of this obvious preponderance of malaria and TB in Africa, there is a very high possibility of an overlap leading to the high incidence of malaria/TB co-infection. Available report shows the prevalence of malaria infection among TB patients to be 1.5%, 2.2%, and 33%.[3-5]

In general, the effect of malaria infection on hematological parameters has been reported to include reduction in eosinophils, neutrophils, total white blood cell (TWBC) count, red blood cell (RBC) count, hemoglobin, hematocrit, plateletcrit, platelet count and an increase in mean cell volume, mean cell hemoglobin, mean cell hemoglobin concentration, neutrophil to lymphocyte ratio (NLR), monocyte to lymphocyte ratio, monocyte count, basophil count, lymphopenia or lymphocytosis in comparison to nonmalaria infected participants.[6-12] Similarly, TB infection has also been reported to cause derangements in hematological parameters ranging from reduced hematocrit, hemoglobin or obvious anemia, reduced lymphocyte count, eosinophil count and mean cell hemoglobin concentration as well as an increase in TWBC count, neutrophil count, platelet count, and erythrocyte sedimentation rate.[13,14] It is likely that these effects may be maintained, suppressed, or potentiated when there is co-infection of TB and malaria. These effects are also likely to be modified at the various stages of anti-tuberculosis (TB) therapy as hematological disorders are known to arise through a variety of mechanisms and etiologies and can be drug induced (drug-induced hematological disorders).[15,16]

A wide range of hematological abnormalities has been reported resulting from the administration of anti-TB drugs. Directly observed treatment (DOTS) short course (DOTS) (also known as TB-DOTS) is the most cost-effective strategy approved by the World Health Organization for the treatment of TB. This standard first-line treatment regimen is separated into two phases. The initial phase called the intensive phase includes the first 8 weeks of treatment and utilizes the potent sterilizing effects of rifampicin (RIF), pyrazinamide (PZA) isoniazid (INH), and ethambutol to clear live bacilli from sputum. The continuation phase is an additional 4 months which utilizes the combination of INH and RIF to eradicates residual organisms and minimize relapse of disease.[17]

Although this treatment eradicates *tubercle bacilli* from the host body, it also causes other adverse side effects such as hepatotoxicity, nephrotoxicity, ototoxicity, thrombocytopenia, neutropenia, immune impairment, and dermatological effects.[18] A number of studies in different locations across the world have investigated the magnitude of anti-TB drug induced changes in leukocytes and other hematological parameters. In Nigeria, Olaniyi and Aken'Ova,[19] reported that the profile of anti-TB drug-induced hematological abnormality was 4.8% lymphopenia, 22.3% leukocytosis, 45.2% neutrophilia, and 93.6% anemia, respectively, while a study in Cameroun reported a 56.45% agranulocytosis, 38.71% leucopenia, 37.1% anemia, and 27.42% thrombocytopenia.[16] In India, the prevalence of drug-induced anemia was 74% together with 26% leukocytosis and 24% thrombocytosis.[20] Putra[21] reported a decrease in platelets, red cell distribution width, granulocytes, monocytes and an increase in hemoglobin, hematocrit, mean cell volume, and eosinophils with anti-TB treatment. Conversely, Bahi *et al*.[22] reported a significantly reduced hemoglobin while another study in Nigeria[23] also found significant variations in hematological parameters with different phases of anti-TB treatment.

The objective of this study was therefore to determine the possible impacts of malaria co-infection on leukocyte indices of TB-infected participants before and during the two phases of first-line anti-TB treatment (intensive and continuation phase). We hypothesized that the hematological parameters will differ in TB participants co-infected with malaria at the different phase of treatment. Understanding the possible impacts of malaria co-infection on leukocyte indices of TB participants at different phases of therapy may help to define the hematological changes to expect when TB infection is complicated with malaria infection before treatment, at intensive and continuation phase of treatment.

Materials and Methods

Study design

This is a cross-sectional study designed to assess the impact of malaria co-infection on leukocyte indices of TB-infected individuals at pre-treatment, intensive phase and continuation phase anti-TB treatment. A total of 180 participants were recruited comprising 60 treatment-naïve participants (35 TB infected and 25 TB/malaria infected), 60 participants that have completed intensive phase treatment (36 TB infected and 24 TB/malaria infected) and 60 participants that have completed continuation phase of treatment (27 TB infected and 33 TB/malaria infected). The intensive phase treatment regimen consists of a fixed dose combination of RIF, INH, PZA, and ethambutol for 2 months, whereas the continuation phase treatment

regimen consists of combination of RIF and INH for additional 4 months. The participants were enlisted after the completion of each phase of treatment (at the 2nd month and 6th month, respectively). The study was carried out between October 2018 and December 2019.

Study setting

This study was carried out at the TB Center of Mile Four Hospital, a Special TB and Leprosy Referral Center located in Abakaliki, Ebonyi State, Nigeria. Abakaliki is the capital of Ebonyi state in South-east geopolitical zone of Nigeria. The hospital is a mission hospital equipped for the management of TB infection with support from donor agencies.

Sample size determination

Sample size was calculated using G*Power software version 3.0.10 (Universitat Dusseldorf Germany). A power analysis using G-power software showed that a total sample size of 180 was needed to achieve a power of 85 at an alpha level of 0.05.

Participant recruitment

The study population was adult (male and female) smear and GeneXpert positive pulmonary TB patients who completed the intensive and continuation phase of treatment at the TB clinic of Mile Four hospital during the study period. The participants that meet the inclusion criteria were recruited consecutively to make up the sample size. Participants positive for active pulmonary *Mycobacterium tuberculosis* and co-infected with malaria as well as TB participants not infected with malaria were included, while participants with any known bleeding disorders or history of bleeding, pregnant women, participants that had blood transfusion in the previous 3 months, participants on aspirin and anticoagulant therapy, females on oral contraceptives, smokers, those taking any local herbs or herbal concoctions, participants that have other known clinical diseases such as cancer, HIV, diabetes, chronic kidney, and liver diseases were excluded from the study.

Ethical considerations

Ethical approval was obtained from the Ethics committee of Federal Teaching Hospital Abakaliki (FETHA/REC/VOL2/2018/105), and permission was sought and obtained from the management of Mile four hospital Abakaliki before sample collection. The modalities for the research were explained to prospective participants and those who gave oral consent were recruited into the study, and confidentiality was ensured by maintaining anonymity in compliance with the Helsinki Declaration.

Blood sample collection

Three milliliters of blood was collected from each subject and processed ensuring the integrity of cellular elements and avoiding preanalytical errors arising from sample collection and processing. It was dispensed into bottles containing di-potassium ethylenediamine tetra-acetic acid (K_2-EDTA) at a concentration of 1.5 mg/ml of blood and used for full blood count as well as malaria parasite diagnosis and parasite count.

Sputum for tuberculosis diagnosis

Two sputum samples (consisting of one spot sample and one early morning sample) collected in a wide mouth container from the participants was used for acid-fast bacilli test as well as for the automated GeneXpert MTB/RIF real-time nucleic acid amplification test for rapid and simultaneous detection of TB and RIF resistance.

Methods of sample analysis

Diagnosis of tuberculosis

This was done by Ziehl–Neelsen technique for *Mycobacterium tuberculosis* diagnosis and GeneXpert method for the detection of *Mycobacterium tuberculosis* and RIF resistance (GeneXpert MTB/RIF).

Diagnosis of malaria and malaria parasite count

Whole blood was used for the diagnosis of malaria using thick and thin blood smears for microscopic detection. The malaria parasite counts were done using thick blood films as described by the WHO.[24]

Body mass index

A well-calibrated weighing scale was used for weight measurements. Care was taken that the weighing scale was zeroed before weight measurement. The participants were instructed to remove footwear and climb barefooted unto the scale. The weight was then read off and recorded in kilograms.

A metre rule calibrated in meters was used to measure the heights of the participants. The participants were asked to remove foot wear before the measurement. Heights were recorded in meters.

The body mass index (BMI) for each subject was then calculated by dividing the weight by the square of the height in meters (kg/m^2).

Total white cell count

A 1 in 20 dilution of well mixed EDTA blood was made by adding 20 µl of blood to 0.38 ml of Turks solution in a small glass tube. The tube was corked and the diluted blood sample mixed. Using a capillary tube, one of the grids of the chamber was loaded with the sample. Precaution was taken not to overfill the chamber. The chamber was left undisturbed for 2 min to allow the white cells to settle. Using ×40 objective, the cells in the four large corners were counted.

The number of white blood cell (WBC) obtained was calculated as follows;

Total number of cells counted × dilution factor/volume counted (μl)

Differential white cell count

Thin blood films were made from EDTA anticoagulated blood and air dried. The air dried slides were covered with Leishman stain using a dropper and was left for 3 min. Twice the volume of pH 6.8 buffered water was added and allowed to further stain for 10 min. The stain was washed off; the back of the slide wiped clean and was placed on a draining rack to dry. Using oil immersion, the slide was viewed and white cells differentiated and counted. A total of 100 WBC s were counted.

Packed cell volume

Plain capillary blood was filled up to three quarters with well mixed EDTA anticoagulated blood. The unfilled end was heat-sealed with the flame of a Bunsen burner, while rotating the end of the capillary in the flame. The sealed capillary was placed in one of the numbered slots in the microhematocrit rotor with the sealed end against the rim gasket. The inner lid was closed. It was centrifuged for 5 min at 12000 g, and the packed cell volume (PCV) was read using the PCV reader.

Platelet count

A 1 in 20 dilution of well mixed blood was made in diluent by adding 20 μl of blood to 0.38 ml of ammonium oxalate (10 g/l). Before the dilution, the blood sample was examined to rule out the presence of any blood clot. The suspension was mixed properly and an improved Neubauer counting chamber was filled with the suspension using a Pasteur pipette. The counting chamber was placed in a moist Petri dish and left untouched for 20 min to give time for the platelets to settle. The preparation was examined using ×40 objective.

The platelet count was determined as follows;

Platelet count per liter = No of cells counted × dilution/volume counted (μl).

Statistical analysis

The Statistical Package for the Social Sciences software (IBM Corp., Armonk, NY, USA) version 22 was used in the statistical analysis. A normality test was conducted to assess the distribution of each variable using Kolmogorov–Smirnov statistic. Data were normally distributed and thus were expressed as mean ± standard deviation. Independent-samples *t*-test was used for the comparison between malarial parasite infected and noninfected groups at pretreatment, after intensive phase of treatment and after continuation phase of treatment and Pearson's product-moment correlation was used to test relationship between mean parasite count (MPC) and the other variables. $P < 0.05$ was considered statistically significant.

Results

Majority of the TB/MP-infected and TB-infected participants were males (109 subjects) with fewer females (71 participants) [Table 1].

At pretreatment, the mean total white cell count ($\times 10^9$/l), mean absolute neutrophils count ($\times 10^9$/l), absolute lymphocyte count ($\times 10^9$/l), NLR, and mean platelet count ($\times 10^9$/l) were significantly lower in TB participants co-infected with malaria (TB/MP+) compared with to TB participants without malaria (TB/MP-) ($P = 0.041$, 0.022, 0.046 and 0.026, respectively). Conversely, the mean eosinophil count ($\times 10^9$/l) was significantly higher in TB/MP + compared with TB/MP-($P = 0.043$) [Table 2].

After intensive phase treatment, there was no significant difference in the mean values of BMI and other hematological parameters when compared between TB/MP+ and TB/MP-($P > 0.05$) [Table 3].

After continuation phase treatment, the mean eosinophil count ($\times 10^9$/l) was significantly higher in TB/MP+ compared with TB/MP, while the mean PCV (l/l) was significantly lower in TB/MP+ compared with TB/MP-($P = 0.045$ and 0.046, respectively) [Table 4].

Correlation analysis shows that at pretreatment, there was a significant moderate positive correlation between MPC and monocyte count ($r = 0.629$; $P < 0.001$), neutrophil count ($r = 0.693$; $P < 0.001$) and lymphocyte count ($r = 0.609$; $P < 0.001$), respectively, and a strong significant positive correlation between MPC and total WBC count ($r = 0.775$; $P < 0.001$) as well as a weak significant positive correlation between MPC and eosinophil count ($r = 0.440$; $P = 0.017$). Similarly, after intensive phase treatment, there was a significant moderate positive correlation between MPC and monocyte count ($r = 0.577$; $P = 0.001$), neutrophil count ($r = 0.709$; $P < 0.001$), lymphocyte count ($r = 0.652$; $P < 0.001$), and a strong significant positive correlation between MPC and total WBC count ($r = 0.770$; $P < 0.001$) as well as a moderate negative correlation between MPC and platelet count ($r = -0.599$; $P = 0.022$). Moreover, after continuation phase treatment, there was a significant moderate positive correlation between MPC and neutrophil count ($r = 0.607$; $P < 0.001$), lymphocyte count ($r = 0.568$; $P < 0.001$), and total WBC count ($r = 0.636$; $P < 0.001$) [Table 5].

Table 1: Gender distribution of the tuberculosis participants with and without malaria

Gender distribution	Pretreatment (*n*=60)		Intensive phase (*n*=60)		Continuation phase (*n*=60)		Total
	TB/MP-infected participants	TB-infected participants	TB/MP-infected participants	TB-infected participants	TB/MP-infected participants	TB-infected participants	
Males	15	21	15	23	19	16	109
Females	10	14	9	13	14	11	71
Total	25	35	24	36	33	27	180

TB=Tuberculosis, MP=Malaria parasite

Table 2: Comparison of mean levels body mass index and hematological parameters between tuberculosis participants with and without malaria infection before treatment

Parameters	TB/MP+ (*n*=25)	TB/MP− (*n*=35)	*t*	*P*
TWBC (×10⁹/l)	10.89±5.10	12.52±5.16	−2.091	0.041*
NEUT (×10⁹/l)	6.29±3.42	7.75±4.28	−2350	0.022*
LYM (×10⁹/l)	3.53±1.87	4.46±2.04	−1.964	0.046*
MONO (×10⁹/l)	0.40±0.31	0.37±0.24	0.486	0.629
EOS (×10⁹/l)	0.09±0.10	0.06±0.11	2.045	0.043*
NLR	1.45±0.58	1.85±1.00	−2.133	0.036*
MLR	0.10±0.08	0.09±0.06	0.554	0.582
PLT (×10⁹/l)	228.17±116.59	275.14±99.09	−2.230	0.026*
PCV (l/l)	0.33±0.06	0.33±0.05	0.078	0.938
BMI (kg/m)	20.05±2.83	18.82±1.67	1.939	0.059

*P<0.05=Significant. TB/MP+=TB participants co-infected with MP, TB/MP−=TB participants not co-infected with MP. TWBC=Total white blood cell count, NEUT=Absolute neutrophils count, LYM=Absolute lymphocytes count, MONO=Absolute monocytes count, EOS=Absolute eosinophils count, PCV=Packed cell volume, BMI=Body mass index, NLR=Neutrophil lymphocyte ratio, MLR=Monocyte lymphocyte ratio, PLT=Total platelet count, TB=Tuberculosis, MP=Malaria parasite

Table 3: Comparison of mean levels body mass index and hematological parameters between tuberculosis participants with and without malaria infection after intensive phase treatment

Parameters	TB/MP+ (*n*=24)	TB/MP− (*n*=36)	*t*	*P*
TWBC (×10⁹/l)	5.43±1.65	5.37±1.59	0.154	0.878
NEUT (×10⁹/l)	2.89±0.97	2.85±0.97	0.189	0.851
LYM (×10⁹/l)	2.35±0.82	2.42±0.87	−0.348	0.729
MONO (×10⁹/l)	0.16±0.08	0.18±0.11	−0.623	0.538
EOS (×10⁹/l)	0.03±0.04	0.03±0.04	−0.012	0.990
NLR	1.28±0.36	1.24±0.30	0.442	0.660
MLR	0.07±0.04	0.08±0.05	−0.341	0.734
PLT (×10⁹/l)	275.71±100.69	278.33±91.83	−0.112	0.911
PCV (l/l)	0.35±0.06	0.34±0.05	0.708	0.481
BMI (kg/m²)	20.61±2.31	20.72±3.25	−0.162	0.872

*P<0.05=Significant. TB/MP+=TB participants co-infected with MP, TB/MP−=TB participants not co-infected with MP. TWBC=Total white blood cell count, NEUT=Absolute neutrophils count, LYM=Absolute lymphocytes count, MONO=Absolute monocytes count, EOS=Absolute eosinophils count, PCV=Packed cell volume, BMI=Body mass index, NLR=Neutrophil lymphocyte ratio, MLR=Monocyte lymphocyte ratio, PLT=Total platelet count, TB=Tuberculosis, MP=Malaria parasite

Discussion

We investigated the possible impacts of malaria co-infection on leukocyte indices of TB-infected participants before and during the two phases of anti-TB treatment. The findings shows that before initiation of anti-TB treatment, in TB participants co-infected with malaria, there was a significant reduction in total white cell count, neutrophil count, lymphocyte count, and NLR compared to TB-infected participants without malaria. According to a previous study, malaria-induced changes in the differential white cell counts are very diverse and contradictory and include leucopoenia, lymphopenia, lymphocytosis, the presence of atypical lymphocytes, monocytosis, neutropenia, neutrophilia, immature neutrophils (band cells), eosinopenia, eosinophilia, and leukemoid reactions.[25] The decreased lymphocyte levels during malaria co-infection have been attributed to the reallocation of cells to deep lymphoid organs or by parasite induced apoptosis of human mononuclear cells.[26] Furthermore, the significant reduction observed in WBC counts, neutrophil count, and lymphocyte count agrees with the work of Kotepui *et al*.,[8] but their finding of a significant higher NLR disagrees with our finding.

The eosinophil count was significantly higher in malaria co-infected TB participants both at pretreatment and after continuation phase treatment. This is expected since eosinophils are known to play a major role in parasitic infections and malaria-TB co-infection may not be an exception. The major function of eosinophil as a cytotoxic cell is against parasitic infections and eosinophils can kill a wide variety of parasitic organism, especially in their larval stages.[27] Furthermore, induction of eosinophils has been attributed to the various factors such as higher release of eosinophils caused by *Plasmodium* or a direct response to the parasite, stimulation by cytokines, or other mediators produced during malaria attack. However, our finding also disagrees with that of Kotepui *et al*.[8] that found a low eosinophil count attributed to malaria suppression of eosinophil production and release from the bone marrow or enhanced the peripheral removal of these cells.

PCV was significantly lower in malaria co-infected TB participants after continuation phase treatment. The reduction in PCV during malaria co-infection may result from the fact that the parasites' primary target is the RBC resulting in RBC destruction, accelerated removal of both parasitized and nonparasitized, and bone marrow dysfunction. Malaria causes the excessive destruction of RBCs during the parasites life cycle because there is the parasitization of red cells by the malaria parasite which leads to shortened survival or death of erythrocytes.

Anemia is a very common presentation of malaria due to direct depression of erythropoiesis by malarial infection and the actual parasitization of red cells by the malaria parasite leading to shortened survival or death of erythrocytes.[28]

The platelet count was significantly lower in malaria parasite-infected TB participants at pretreatment. Malaria infections are commonly accompanied by a thrombocytopenia or loss of platelets, the severity of which closely mirrors the increasing parasite mass.[29] The underlying causes of the reduction in platelet count in malaria infection have been variously attributed to systemic platelet activation, immune-mediated clearance, and vascular pooling.[30] The reduction in platelet count in malaria co-infected TB participants at pretreatment in this study may also be related to the finding of Kho *et al*.[31] that platelet-erythrocyte complexes (which results from the preferential binding of platelet to infected erythrocytes more than uninfected erythrocytes) makes up a major proportion of the total platelet pool in patients with malaria and may therefore contribute considerably to malarial thrombocytopenia. Similarly, the reduction in platelet count may also be linked to the role of platelet in the innate control of Plasmodium infection in human malaria that involves the control of the growth of intra-erythrocytic *Plasmodium* parasites by directly binding to infected erythrocytes and killing the parasite inside via the action of platelet factor-4.[31] This process results in the utilization of platelet in parasite killing that result in the decrease in peripheral circulation. However, our findings disagree with that of Aisha *et al*.[32] that found an increase in platelet count which they attributed to platelet activation resulting from malaria parasite infection because in addition to their well-defined role in hemostasis, platelets are increasingly implicated in immunological processes, including direct pathogen-killing functions.[33] We also observed a significant moderate negative correlation between MPC and platelet count which also agrees with the report of Kho *et al*.[31]

Table 4: Comparison of mean levels body mass index and hematological parameters between tuberculosis participants with and without malaria infection after continuation phase treatment

Parameters	TB/MP+ (*n*=33)	TB/MP− (*n*=27)	*t*	*P*
TWBC (×10⁹/l)	6.53±2.52	6.67±2.78	−0.220	0.827
NEUT (×10⁹/l)	3.60±1.60	3.46±1.48	0.383	0.703
LYM (×10⁹/l)	2.56±1.02	2.83±1.12	−1.044	0.300
MONO (×10⁹/l)	0.21±0.14	0.19±0.14	0.556	0.580
EOS (×10⁹/l)	0.07±0.07	0.04±0.06	1.976	0.045*
NLR	1.38±0.46	1.24±0.33	1.433	0.157
MLR	0.09±0.06	0.08±0.06	0.640	0.524
PLT (×10⁹/l)	343.61±64.92	336.65±79.82	0.378	0.707
PCV (l/l)	0.30±0.06	0.33±0.05	−1.958	0.046*
BMI (kg/m²)	21.73±2.84	21.72±3.13	0.022	0.983

*P<0.05=Significant. TB/MP+=TB participants co-infected with MP, TB/MP−=TB participants not co-infected with MP. TWBC=Total white blood cell count, NEUT=Absolute neutrophils count, LYM=Absolute lymphocytes count, MONO=Absolute monocytes count, EOS=Absolute eosinophils count, PCV=Packed cell volume, BMI=Body mass index, NLR=Neutrophil lymphocyte ratio, MLR=Monocyte lymphocyte ratio, PLT=Total platelet count, TB=Tuberculosis, MP=Malaria parasite

CONCLUSION

Malaria co-infection induces a reduction in WBC parameters (total count, lymphocyte, neutrophil count, and NLR) and platelet count in TB participants before initiation of treatment aside from eosinophils count which was increased before treatment and after continuation phase treatment. Thus, the effect of malaria co-infection on the parameters varied with the different stage of treatment, thereby suggesting that the anti-TB treatment altered the effect of malaria co-infection on these parameters.

The strength of this study is that it considered the various phases of anti-TB therapy. However, it has the limitation that it was a cross-sectional study in which the individual participants were not followed up in the course of treatment.

Acknowledgment

We would like to thank the management and staff of Mile Four hospital Abakaliki for their contribution to this research work.

Table 5: Correlation of mean parasite count and hematological parameters in tuberculosis participants co-infected with malaria

Parameters	Pretreatment		Intensive phase		Continuation phase	
	r	*P*	*r*	*P*	*r*	*P*
MPC versus EOS	0.440*	0.017	−0.030	0.880	0.004	0.982
MPC versus MONO	0.629*	<0.001	0.577*	0.001	0.265	0.103
MPC versus NEUT	0.693*	<0.001	0.709*	<0.001	0.607*	<0.001
MPC versus LYM	0.609*	<0.001	0.652*	<0.001	0.568*	<0.001
MPC versus TWBC	0.775*	<0.001	0.770*	<0.001	0.636*	<0.001
MPC versus PLT	−0.177	0.358	−0.599*	0.022	−0.047	0.784

*P<0.05=Significant. TB/MP+=TB participants co-infected with MP, TB/MP−=TB participants not co-infected with MP. TWBC=Total white blood cell count, NEUT=Absolute neutrophils count, LYM=Absolute lymphocytes count, MONO=Absolute monocytes count, EOS=Absolute eosinophils count, PCV=Packed cell volume, BMI=Body mass index, NLR=Neutrophil lymphocyte ratio, MLR=Monocyte lymphocyte ratio, PLT=Total platelet count, TB=Tuberculosis, MP=Malaria parasite

Financial support and sponsorship

This study was financially supported by Tertiary Education Trust Fund (TETFUND), Nigeria.

Conflicts of interest

There are no conflicts of interest.

References

1. World Health Organization, World Malaria Report, 2018.
2. World Health Organization, Global Tuberculosis Report, World Health Organization, 2018.
3. Irene AA, Enekembe MA, Meriki HD, Fonkeng NF, Nkuo-Akenji T. The effect of Malaria/HIV/TB triple infection on malaria parasitaemia, haemoglobin levels, CD4+cell and acid fast bacilli counts in the south west region of Cameroon. J Infect Pulm Dis 2016;2:2470-3176.
4. Baluku JB, Nassozi S, Gyagenda B, Namanda M, Andia-Biraro I, Worodria W, *et al*. Prevalence of Malaria and TB coinfection at a National Tuberculosis Treatment Centre in Uganda. J Trop Med 2019; 2019:1-7.
5. Attahiru A, Bashir A, Mukhtar GL. Prevalence of malaria parasites among tuberculosis patients attending Specialist Hospital, Gombe State, Nigeria. UMYU J Microbiol Res 2016;1:184-8.
6. Mutala AH, Badu K, Owusu C, Agordzo SK, Tweneboah A, Abbas DA, *et al*. Impact of malaria on haematological parameters of urban, peri-urban and rural residents in the Ashanti region of Ghana: A cross-sectional study. AAS Open Res 2019;2:27.
7. Sakzabre D, Asiamah EA, Akorsu EE, Abaka-Yawson A, Dika ND, Kwasie DA, *et al*. Haematological Profile of Adults with Malaria Parasitaemia Visiting the Volta Regional Hospital, Ghana. Adv Hematol. 2020;2020:9369758. doi: 10.1155/2020/9369758. PMID: 32095139; PMCID: PMC7036090.
8. Kotepui M, Phunphuech B, Phiwklam N, Chupeerach C, Duangmano S. Effect of malarial infection on haematological parameters in population near Thailand-Myanmar border. Malar J 2014;13:218.
9. Omarine Nlinwe N, Nange TB. Assessment of hematological parameters in malaria, among adult patients attending the Bamenda Regional Hospital. Anemia 2020; vol 2020:1-8.
10. Bunza NM, Kumurya AS, Muntari B, Isah AA, Kalgo MU. Effect of falciparum malaria on haematological parameters in malaria infected patients in Sokoto Metropolis. Asian Hematol Res J 2019;2:1-8.
11. Adamu J, Jigam AA. Effects of malaria infection on some haematological and biochemical parameters in the general population and pregnant malaria patients attending two district hospitals in Niger State, Nigeria. Glob J Infect Dis Clin Res 2019;5:1-5.
12. Awoke N, Arota A. Profiles of hematological parameters in *Plasmodium falciparum* and *Plasmodium vivax* malaria patients attending Tercha General Hospital, Dawuro Zone, South Ethiopia. Infect Drug Resist 2019;12:521-7.
13. Javed I, Javed MT, Mahmood Z, Riaz M, Iqbal R. Hematological profiling of tuberculosis infected and co-morbid patients: A study carried out in central Punjab, Pakistan. Eur J Inflamm 2018;16:1-6.
14. Kahase D, Solomon A, Alemayehu M. Evaluation of peripheral blood parameters of pulmonary tuberculosis patients at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia: Comparative study. J Blood Med 2020;11:115-21.
15. Kassa E, Enawgaw B, Gelaw A, Gelaw B. Effect of anti-tuberculosis drugs on hematological profiles of tuberculosis patients attending at University of Gondar Hospital, Northwest Ethiopia. BMC Hematol 2016;16:1.
16. Enoh JE, Pokam BD, Eyo AO, Okafor IM, Nguedia JC. Drug induced hematological disorders in patients on antituberculosis drugs in the South west region of Cameroon. EJPMR 2017;4:155-61.
17. Dobbs TE, Webbs RM. Chemotherapy of tuberculosis. In: Scholossberg D, editor. Tuberculosis and Non-tuberculosis Mycobacterial Infections. 6th ed. Washington DC: ASM Press; 2011. p. 107-19.
18. Yang TW, Park HO, Jang HN, Yang JH, Kim SH, Moon SH, *et al*. Side effects associated with the treatment of multidrug-resistant tuberculosis at a tuberculosis referral hospital in South Korea: A retrospective study. Medicine (Baltimore) 2017;96:e7482.
19. Olaniyi JA, Aken'Ova YA. Haematological profile of patients with pulmonary tuberculosis in Ibadan, Nigeria. Afr J Med Med Sci 2003;32:239-42.
20. Yaranal PJ, Umashankar T, Harish SG. Hematological profile in pulmonary tuberculosis. Inter J Health Rehab Sci 2013;2:50-5.
21. Putra PM. Effect of anti-tuberculosis multi drug resistance regimen on hematological lung tuberculosis patients profile with multi drug resistance. Berkala Kedokteran 2018;14:59-68.
22. Bahi GA, Bamba A, M'Boh GM, Aké-Edjeme A, Méité S. Evaluation of the hematological and biochemical markers of Iron metabolism in pulmonary multidrug-resistant tuberculosis (MDR-TB). J Trop Med Health 2018;10:132.
23. Obeagu EI, Okoroiwu IL, Nwanjo HU, Nwosu DC. Evaluation of haematological parameters of tuberculosis patients in Umuahia. EJPMR 2019;6:693-9.
24. World Health Organization. Malaria parasite counting. Malaria Microscopy Standard Operating Procedure (MM-SOP-09). 2016; Available from: www.wpro.who.int.lab-quality. [Last accessed on 2019 Aug 20].
25. Taylor WR, Widjaja H, Basri H, Ohrt C, Taufik T, Tjitra E, *et al*. Changes in the total leukocyte and platelet counts in Papuan and non Papuan adults from northeast Papua infected with acute *Plasmodium vivax* or uncomplicated *Plasmodium falciparum* malaria. Malar J 2008;7:259.
26. Rodrigues-da-Silva RN, Lima-Junior Jda C, Fonseca Bde P, Antas PR, Baldez A, Storer FL, *et al*. Alterations in cytokines and haematological parameters during the acute and convalescent phases of *Plasmodium falciparum* and *Plasmodium vivax* infections. Mem Inst Oswaldo Cruz 2014;109:154-62.
27. Huang L, Appleton JA. Eosinophils in helminth infection: Defenders and dupes. Trends Parasitol 2016;32:798-807.
28. Ajibola M, Oloruntoba AC, Yetusoko ND. Evaluation of PCV and hemoglobin variations among malaria positive and malaria negative patients, at the Ecwa community Health Centre Bukuru, Jos Nigeria. IOSR J Pharm 2012;2:65-9.
29. Hanson J, Phu NH, Hasan MU, Charunwatthana P, Plewes K, Maude RJ, *et al*. The clinical implications of thrombocytopenia in adults with severe falciparum malaria: A retrospective analysis. BMC Med 2015;13:97.
30. Coelho HC, Lopes SC, Pimentel JP, Nogueira PA, Costa FT, Siqueira AM, *et al*. Thrombocytopenia in *Plasmodium vivax* malaria is related to platelets phagocytosis. PLoS One 2013;8:e63410.
31. Kho S, Barber BE, Johar E, Andries B, Poespoprondjo JR. Platelets kill circulating parasites of all major *Plasmodium* species in human malaria. Blood 2018;132:1332-44.
32. Aisha AE, Mayssa MZ, Manal K, Ahmed N, El-Sayed A, Walid E. Plasma concentration of platelet factor 4: As an evidence of platelet activation in parasitic infections. Res J Parasitol 2012;7:25-31.
33. Ali RA, Wuescher LM, Dona KR, Worth RG. Platelets mediate host defense against *staphylococcus aureus* through direct bactericidal activity and by enhancing macrophage activities. J Immunol 2017;198:344-51.