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Changes in Some Hematological Parameters of Female Patients on Directly Observed Treatment Short-Course (DOTS) in a Tuberculosis Hospital in Bayelsa State, Nigeria

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ABSTRACT

Introduction: Tuberculosis disease remains a health challenge globally. Anti-TB drugs are not completely free from side effects. **Objective**; This study was aimed at determining the effect/s of first and second line Directly Observed Treatment Short-course (DOTS) therapy on the selected hematological parameters of female TB infected patients. **Materials and methods**. The longitudinal study involved 198 female subjects attending a TB hospital in Bayelsa State, Nigeria. AFB test was done using Zeihl-Neelson technique, ESR by the westerngreen method and hematological parameters analyzed with the Abacus 380 Hematology Autoanalyzer. ANOVA was used to compare the mean values and SPSS version 20.00 was employed to analyze the data. **Results**: Results from the study indicate that there was significant difference in most parameters when control values were compared with that of the newly infected TB subjects. They include; WBC (p=0.0001), RBC (p=0.0001), HB (p=0.0001), PCV (p=0.0001) and ESR (p=0.0001). On the post-hoc involving control/second line treatment subjects, five items yielded insignificant values; WBC, RBC, PCV, HB and MCH. **Conclusion**: While our study showed that TB disease significantly affected all the parameters, there was a real improvement in the treatment stage as all parameters were returning back to normal values. This suggests that as time progresses absolute normalization can occur. It is inferred from this that the DOTS chemotherapy has no negative effect on the hematopoietic process. We therefore suggest further studies that will look into the plasma components of patients undergoing DOTS chemotherapy.

Key words; Anti-TB Therapy, DOTS, Hematological Parameters,

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INTRODUCTION

Tuberculosis also known as TB, is a major health issue and a principal infectious killer disease. It is caused mainly in man by the parasite *Mycobacterium tuberculosis*. The bacillus enters the body by breathing of droplets or dust particles containing it. It occurs as pulmonary tuberculosis or non-pulmonary tuberculosis(1). It is known globally that 700 000 women die from tuberculosis every year; this infectious ailment kills more females than do all causes of maternal mortality combined.

In Africa (especially sub-Saharan Africa), cases of tuberculosis have grown dramatically, overpowering control programs (2). This negative effect could be due to the fact that tuberculosis infection control interventions are not routinely implemented as against what happens in high income countries with low prevalence of tuberculosis where infection control policies are routinely observed(3). However, the launch of the Directly Observed Treatment Short-course (DOTS) in 1995 by the World Health Organization (WHO) has shown to be an actual intervention that will lead to reduced tuberculosis transmission and lessening number of tuberculosis cases(4)(5). Reports have shown that it is among the most economical global health interventions available today(6)(7). DOTS was first implemented in India in the year 1958. It is made up of five components which include (1) government obligation to control activities. (2) Case detection by sputum smear microscopy. (3) Standardized treatment regiments lasting at 6 – 8 months directly observed for 2 months. (4) Regular and continual provision of anti-TB drugs and (5) standardized recording and reporting system. The major objective behind this strategy is to form a close relationship between patients and health workers or volunteers in order to help them successfully complete treatment, and to avert drug resistance (8). DOTS extension and improvement remains one of the vital tactics adopted by the National TB and Leprosy Control Program to the realization of a general access to TB services in Nigeria (9).

Several research works have revealed significant alterations in hematological parameters amongst subjects with new cases of TB compared with healthy subjects **(10, 11, 12, 13, 14, 15, 16).** However, there are very few researches that describes the **hematological** parameters of infected females throughout the 6 or 9-month period of administration of the DOTS treatment with only some centering only on the first line course of therapy (17)(18). This study was aimed at determining the effect of first line and second line DOTS therapy on the **hematological** parameters of Pulmonary TB infected female patients.

MATERIALS AND METHODS

Subjects and Setting

A Longitudinal study design was adopted in this study; involving 198 female subjects. Subjects were congregated into four (4) groups: (1) Apparently healthy control subjects, (2) Newly diagnosed TB subjects, (3) First line (Intensive Phase) DOTS treatment (Isoniazid, Rifampin, Pyrazinamide and Ethambutol) subjects who are at the end of their second (2^{nd}) month treatment and (4) Second line (Continuation Phase) DOTS treatment (Rifampisin and Isoniazide), subjects who are at the end of their six (6^{th}) month treatment. Their ages ranged from 25 to 50 years. Smokers, alcohol consumer, persons with septic wounds, people with diabetes and other chronic illness, were excluded from the study. The study was carried out at the Tuberculosis and leprosy Hospital Igbogene, Yenagoa Local

Government Area of Bayelsa State Nigeria. Authorization for the study was gotten from the ministry of Health Bayelsa State Nigeria with ethical approval number BSMoHEC/2018/015 on 21st October 2018.

Blood Sample Collection

Blood sample was collected as described by Ochei and Kolhatkar (1). Five (5) ml of venous blood was collected from each of the subjects and carefully put into Ethylene Diamine Tetra Acetic **acid** (EDTA) containers. After proper mixing, the samples were analyzed.

Tuberculosis Test: The Ziehl Neelsen method was used to detect Acid Fast Bacilli (AFB). Infection was confirmed by microscopic identification of tuberculosis bacilli in stained sputum smear (1).

Full Blood Count Analysis

Full Blood Count Analysis was done with the Abacus 380 Hematology Auto analyzer. The items analyzed were White Blood Count (WBC), Red Blood Count (RBC), Packed Cell Volume (PCV) red cell indices of Mean Cell Volume (MCV), Mean Cell Hemoglobin (MCH) and Mean Cell Hemoglobin Concentration and hemoglobin estimation (HB). The operating principle of this analyzer is the impedance or coulter method (19). In this method, individual cell is suspended in a conductive diluent acts as an insulator. As the cells go through an aperture, they increase the resistance of the electrical path between the submerged electrodes on either side of the aperture. Consequently, a measurable electronic pulse is generated. The number of pulses is proportional to the number of cell particles, and cell volume (20).

For the Hemoglobin measurement, the sample is lysed, diluted and measured by photometry. The lytic process releases hemoglobin. This hemoglobin is converted chemically, to methemoglobin which is measured by a photometer in the chamber (19).

Erythrocyte Sedimentation Rate (ESR)

ESR was estimated by the westerngreen method (1).

Statistical analysis:

Data collected from this research work was analyzed with **SPSS version 20.00** software. The inferential statistics Analysis of Variance (ANOVA) was employed to compare the parameters under study. A p value of less than 0.05 ($p<0.05$) was considered significant.

RESULTS

The total number who partook in the study was 198 female subjects. They were clustered into four categories: Control group (58), New cases (38) First line treatment group (36) and Second Line treatment TB subjects (66) (Figure 1). Their age ranged from 25 to 50 years. For all groups. Scientific comparisons were made between each group.

Figure 1. Distribution of subjects

In Table 1., the mean values for all categories is compared using Analysis of variance (ANOVA). One (1) parameter had insignificant p values while the rest seven (7) had significant p values. The insignificant one is; MCH (f = 0.70 and p = 0.5590). The others with significant values include RBC (f = 8.081 and p = 0.0001), ESR (f = 37.45 and p = 0.0001), MCV (f = 443.19 and p = 0.0001), PCV (f = 9.865 and p = 0.0001), HB (f = 8.509 and p = 0.0001), MCHC (f = 18.38 and p = 0.0001) and lastly WBC (f= 27.02 and p= 0.0001).

Table 1a. Comparison of Mean ± SD of Hematological Parameters among Control, New cases, First line and Second line female subjects in TB treatment.

Parameter		Control Subjects	New cases	First line	Second line	f, df	p-value
	N =	58	38	36	66		
WBC(x10^9/L)	Mean±SD	6.16±1.38	8.67±2.44	6.57±1.36	5.69±1.56	27.02,3	0.0001*
RBC(x10^{12}/L)	Mean±SD	4.90±0.72	4.28±0.31	4.56±0.71	4.60±0.57	8.081,3	0.0001*
HB (g/dl)	Mean±SD	12.06±1.67	10.36±1.77	11.14±1.85	11.44±1.40	8.509,3	0.0001*
PCV (%)	Mean±SD	36.75±5.41	31.06±5.10	33.72± 6.20	34.97±1.18	9.865,3	0.0001*
ESR (mm/h)	Mean±SD	6.27 ± 1.09	54.36±39.01	61.44±36.76	58.03±36.53	37.45,3	0.0001*
MCV (fl)	Mean±SD	74.90±5.80	72.84± 8.20	74.28± 5.32	78.42±5.52	443.19,3	0.0001*
MCH (pg)	Mean±SD	24.71±1.93	24.02± 2.81	24.39± 1.72	24.43±2.44	0.70,3	0.5590
MCHC (g/dl)	Mean±SD	329.24±6.95	330.53±7.87	328.39±6.96	321.03±8.18	18.38,3	0.0001*

Key: WBC: White Blood Count, RBC: Red Blood Count, HB: Hemoglobin concentration, PCV: Packed Cell Volume, ESR: Erythrocyte Sedimentation Rate, MCV: Mean Cell Volume, MCH: Mean Cell Hemoglobin, MCHC: Mean Cell Hemoglobin Concentration. *Significant value

Table 1b shows the Post Hoc analysis of Control/New cases and Control / First line subjects. The Mean±SD of Control/New cases for WBC, RBC, HB, PCV and ESR are 6.16±1.38/8.67±2.44, 4.90±0.72/4.28±0.31, 12.06±1.67/10.36±1.77, 36.75±5.41/31.06±5.10 and 6.27±1.09/54.36±39.001 respectively. The post-hoc gave a P value of p= 0.0001 for all parameters.

The other parameters i.e. MCV, MCH and MCHC all had insignificant values. For MCV, the Mean±SD of Control/New cases was 74.90±5.80/72.84±8.20. The post-hoc gave a p value of p=0.4900. That of MCH and MCHC are 24.71±1.93/24.02±2.81 and 329.24±6.95/330.53±7.87 with a post- hoc of p= 0.5500 and p = 0.8820 respectively.

The second part of the table is the post hoc of Control/Firstline subjects. The parameters whose comparison of the control and firstline values was significant are ESR (p= 0.0001) and MCV (p = 0.0001). The rest parameters which include WBC, RBC, HB, PCV, MCH and MCHC all had their p values greater than 0.050(0.7190,0.0780, 0.0780, 0.550, 0.9350 and 0.9630 respectively).

Table 1c contains the post hoc analysis of Control/ second line and New cases / First line subjects. On the first part of the table, the control subjects had their WBC values higher than those on second line treatment (6.16±1.38/5.69±1.56). The post hoc analysis gave a p value of p= 0.4920 which is insignificant. Furthermore, it reveals an insignificant p values for RBC (p=0.0690), HB (p=0.2390), PCV (p= 0.2950) and MCH (p= 0.9010). The post hoc values for the other remaining three parameters were significant; ESR (p = 0.0001) MCV (p= 0.0240) and MCHC (p= 0.0001).

The second part of the table gives the post hoc p values for New cases / First line subjects. For WBC, the value for New case is 8.67±2.44 as compared to first line value of 6.57±1.36 which resulted to a significant p-value of p= 0.0001. Another significant p value was seen in MCV (72.84±8.20/74.28±5.32, p=0.0001). The table further reveals all other parameters as having insignificant p values. They include; RBC p = 2870, HB p= 0.2400, PCV p= 0.1770, ESR p= 0.8150, MCH0 p= 9210 and MCHC p= 0.6880.

Table 1b. Post- Hoc analysis of Control/New cases and Control / First line subjects

Parameter		Control Subjects	New cases	p-value	Control Subjects	First line	p-value
	N =	58	38		58	36	
WBC(x10^9/L)	Mean±SD	6.16±1.38	8.67±2.44	0.0001*	6.16±1.38	6.57±1.36	0.7190
RBC(x10^{12}/L)	Mean±SD	4.90±0.72	4.28±0.31	0.0001*	4.90±0.72	4.56±0.71	0.0780
HB (g/dl)	Mean±SD	12.06±1.67	10.36±1.77	0.0001*	12.06±1.67	11.14±1.85	0.0780
PCV (%)	Mean±SD	36.75±5.41	31.06±5.10	0.0001*	36.75±5.41	33.72± 6.20	0.0550
ESR (mm/h)	Mean±SD	6.27 ± 1.09	54.36±39.01	0.0001*	6.27 ± 1.09	61.44±36.76	0.0001*
MCV (fl)	Mean±SD	74.90±5.80	72.84± 8.20	0.4900	74.90±5.80	74.28± 5.32	0.0001*
MCH (pg)	Mean±SD	24.71±1.93	24.02± 2.81	0.5570	24.71±1.93	24.39± 1.72	0.9350
MCHC (g/dl)	Mean±SD	329.24±6.95	330.53±7.87	0.8820	329.24±6.95	328.39±6.96	0.963

Key: WBC: White Blood Count, RBC: Red Blood Count, HB: Hemoglobin concentration, PCV: Packed Cell Volume, ESR: Erythrocyte Sedimentation Rate, MCV: Mean Cell Volume, MCH: Mean Cell Hemoglobin, MCHC: Mean Cell Hemoglobin Concentration. *Significant value

Table 1c. Post Hoc analysis of Control/ second line and New cases / First line subjects

Parameter		Control Subjects	Second line	p-value	New cases	First line	p-value
	N =	58	66		38	36	
WBC(x10^9/L)	Mean±SD	6.16±1.38	5.69±1.56	0.4920	8.67±2.44	6.57±1.36	0.000
RBC(x10^{12}/L)	Mean±SD	4.90±0.72	4.60±0.57	0.0690	4.28±0.31	4.56±0.71	0.2870
HB (g/dl)	Mean±SD	12.06±1.67	11.44±1.40	0.2390	10.36±1.77	11.14±1.85	0.2400
PCV (%)	Mean±SD	36.75±5.41	34.97±1.18	0.2950	31.06±5.10	33.72± 6.20	0.1770
ESR (mm/h)	Mean±SD	6.27 ± 1.09	58.03±36.53	0.0001*	54.36±39.01	61.44±36.76	0.8150
MCV (fl)	Mean±SD	74.90±5.80	78.42±5.52	0.0240*	72.84± 8.20	74.28± 5.32	0.0001*
MCH (pg)	Mean±SD	24.71±1.93	24.43±2.44	0.9010	24.02± 2.81	24.39± 1.72	0.9210
MCHC (g/dl)	Mean±SD	329.24±6.95	321.03±8.18	0.0001*	330.53±7.87	328.39±6.96	0.6880

Key: WBC: White Blood Count, RBC: Red Blood Count, HB: Hemoglobin concentration, PCV: Packed Cell Volume, ESR: Erythrocyte Sedimentation Rate, MCV: Mean Cell Volume, MCH: Mean Cell Hemoglobin, MCHC: Mean Cell Hemoglobin Concentration. *Significant value

Table 1d. Post Hoc analysis of New cases / Second line subjects and First line/Second Line

Parameter		New cases	Second line	p-value	First line	Second line	p-value
	N =	38	66		36	66	
WBC(x10^9/L)	Mean±SD	8.67±2.44	5.69±1.56	0.0001*	6.57±1.36	5.69±1.56	0.0960
RBC(x10^{12}/L)	Mean±SD	4.28±0.31	4.60±0.57	0.0870	4.56±0.71	4.60±0.57	0.9890
HB (g/dl)	Mean±SD	10.36±1.77	11.44±1.40	0.0150*	11.14±1.85	11.44±1.40	0.8470
PCV (%)	Mean±SD	31.06±5.10	34.97±1.18	0.0040*	33.72± 6.20	34.97±1.18	0.7130
ESR (mm/h)	Mean±SD	54.36±39.01	58.03±36.53	0.9540	61.44±36.76	58.03±36.53	0.9640
MCV (fl)	Mean±SD	72.84± 8.20	78.42±5.52	0.0010*	74.28± 5.32	78.42±5.52	0.0001*
MCH (pg)	Mean±SD	24.02± 2.81	24.43±2.44	0.8850	24.39± 1.72	24.43±2.44	1.0000
MCHC (g/dl)	Mean±SD	330.53±7.87	321.03±8.18	0.0001*	328.39±6.96	321.03±8.18	0.0001*

Key: WBC: White Blood Count, RBC: Red Blood Count, HB: Hemoglobin concentration, PCV: Packed Cell Volume, ESR: Erythrocyte Sedimentation Rate, MCV: Mean Cell Volume, MCH: Mean Cell Hemoglobin, MCHC: Mean Cell Hemoglobin Concentration. *Significant value

Table 1d. is the Post-hoc analysis of New cases / Second line and First line/Second Line subjects. In the first part of the table, the WBC had a significant p value of p= 0.0001 when their Mean±SD was compared (8.67±2.44/5.69±1.56). Other parameters with significant p values are HB p= 0.0150, PCV p= 0.0040, MCV, p= 0.0001 and MCHC, p=0.0001. The rest which are RBC, ESR and MCH all had insignificant p values of p= 0.087, 0.9540 and 0.8850 respectively. On the second part of the table (First line/Second), the post-hoc reveals that only two out of the eight parameters had significant values which are p= 0.0001 for MCV and p= 0.0001 for MCHC. Other post hoc values are p= 0.0960 for WBC, p= 98900 for RBC, p= 0.8470 for HB, p= 0.7130 for PCV and p=1.0000 for MCH

DISCUSSION

TB disease is a serious disease of public health concern in third world countries. Much work has not been done about the effects of anti-TB drugs on the hematological parameters in female pulmonary TB patients undergoing DOTS therapy in Nigeria and more so, in the south-south region of the country, Bayelsa State to be precise. The most effective treatment for tuberculosis is the multidrug approach involving a combination of Isoniazid (INH), Rifampin (RIF), Pyrazinamide (PZA) and Ethambutol (EMB) to hamper drug resistance. This blend is highly efficient in treating tuberculosis, but may also lead to toxicity and side effects.

In this research work, a longitudinal approach was taken to check the effects of anti-TB therapy. Control, non-TB infected subjects, newly diagnosed TB subjects, those at the end of First line (intensive phase) treatment and those at the end of second line treatment (Continuation Phase) were all considered. The total white blood cell count (WBC) increased from the control to the newly infected but steadily declined during the treatment period. The ANOVA result gave a significant p value of p=0.0001. Also, the decline in the number of WBCs from the new cases to the second line treatment revealed a significant post- hoc p value between new cases/ first line (p=0.0001) and new case/second line (p=0.0001) The post-hoc analysis gave an insignificant p value (p=0.4920) between control group and end of treatment group (second line). There was a reduction in number towards normal as treatment continues. The increase WBC in the newly infected subjects has been attributed to an immune response to the TB bacilli. This finding correlates with that of Singh *et al*, 2001,(21). The World Health Organization reports that in tuberculosis disease there is constantly a raised count of white cells beyond normal values (leucocytosis). Anti-TB drugs such INH and RIF are known to bring about acute leucocytosis either singly or in combination through an unfamiliar mechanism (22) . The increase encountered may be due to a blend of the infection and drugs.

In contrast to WBC, the values for HB, PCV, RBC, MCV and MCH all decreased from control subjects to newly infected subjects and then began to rise steadily as treatment progresses.

The HB, PCV and RBC of the Newly infected pulmonary tuberculosis patients (10.36 ±1.77g/dl, 31.06±5.10 % and 4.28±0.31 X 10^{12}/L,) was significantly lower ($p<0.05$) than that of control subjects (12.06±1.67g/dl, 36.75±5.41% and 4.90±0.72 X 10^{12}/L). On the other hand, the MCV and MCH lower values were not significant from the control subjects ($p>0.05$). The value for MCHC for control is 329.24±6.95 and is lower than the Newly infected patients with a value of 330.53±7.87 but not significant ($p>0.05$). In 2005, Ajayi et al (23), in their research work reported significant decreases in these parameters of TB patients. A reduction in haemoglobin concentration and by implication PCV, RBC alongside the absolute values (MC, MCH and MCHC) is known as anemia and have been reported in some studies (24,25). The anemia has been classified as normocytic normochromic with all the features of anemia of chronic disorders (26). Ajayi et al. 2005, further states that Pulmonary tuberculosis disease being a chronic disorder, impacts on the hemopoietic system leading to a decrease in erythropoiesis. Various pathogenesis has been advanced in TB-associated anemia, but most investigators have shown suppression of erythropoiesis by inflammatory mediators as a cause of anemia(18) . The drug Rifampin is said to cause erythrocyte death stimulation of Ca^{2+} permeable cation channels, which

facilitates Ca^{2+} entry into RBC from extracellular spaces leading to ceramide production which leads to phagocytosis and apoptosis (27)(28).

It is worthy to note that though there was a decrease in these parameters on the New cases, they were still higher than values from other research works such as that of Ajayi et al 2005 and Nwankwo et al 2005) in Kano and Benin city. Two reasons can be advanced for this; (1) people in this area practice self-medications a lot and the patent medicine stores never hesitates to add hematinics to medicines for every ailment either in the form of capsule or in tonic form. It is believed therefore that these TB patients takes a lot of them as soon as they feel sick. (2) Foods rich in iron are abundant in this area. They include sea foods such as crayfish, fish, snails, periwinkle, prawns etc. which are part of our daily diet. This finding thus denotes that diet of patients to a larger extent plays an important role in the outcome of their hemoglobin concentration.

When RBCs values were compared, a reduction in number was observed on those on 1st line drugs when compared with normal (control) values, however there was an increase on the value of the second line regiment (4.90±0.72, 4.56±0.71 and 4.60±0.57 for control, first line and second line respectively). An insignificant p value was obtained in the post-hoc values of the control and first line subjects (p = 0.0780). Similarly, the post hoc of the control and second line regiment yielded insignificant result (p=0.0690). All other post hoc values were also insignificant; i.e new cases/first line P=0.2870, new cases /second line p= 0.0870 and p= 0.9890 for first line/second line. This result is in consonance with a research by Eyuel *et al* 2016, (18). They reported an increase of RBCs and suggests no negative erythropoietic effect of drugs on the bone marrow since the mean value of the first and second line patients are building up towards normal value meaning recuperation of the subject. The post hoc for HB and PCV followed the same trend with that of RBC save for the post hoc of new cases/second line. They both have significant p values of p=0.0150 and 0.0040 for HB and PCV respectively. The similar results of the trio are expected as they are both interconnected. The mean values of ESR rose from control to first line treatment before coming down at the end of the therapy (6.27±1.09, 54.36±39.01, 61.44±36.76 and 58.03±36.53mm/h respectively). The ESR values of new cases (54.36±39.01 mm/h;) obtained in this study were significantly higher than control values (6.27±1.09 mm/h), p=0.0000. This agrees with previous findings (13, 23, 24, 29). The test is usually carried out as a nonspecific test for a range of pathological conditions which include: systemic inflammatory conditions, acute or chronic infections and neoplastic conditions. In all these illnesses, ESR is mostly elevated. Increase in ESR could be attributed to increased production of acute phase proteins and release of proteins by the causative organism (*M.tuberculosis)* into the circulation (16). Comparison of mean values of ESR with ANOVA gave a significant result of p=0.0000. Similarly, the post hoc gave a p= 0.0000 for control/first line and p=0.0000 for control/second line treatment group. However, all the other post-hoc gave insignificant p values. In this study, the cellular components of blood (which contributes partly to the rate of fall) were seen to be getting close to normal values at the end of treatment. Though the value of ESR is also coming down towards normal at the end of the continuation phase, the significant p value (p=0.0000) in this line of treatment when compared to the control value could be ascribed to other factors such as the constituents of plasma components which were not considered in this study.

This present study shows a reduction in values of MCV and MCH from control to new cases, and then an increase to the second line regimen. The same was not the case for MCHC as the mean value increased from the control to the new cases and then a decrease through the first line to the second line regimen. Despite this no significant differences ($p>0.05$) were gotten from the post hoc between control and other parameters except for MCV and MCHC in the second line of treatment. The values of the two treatment groups (first line/second line) when compared was significant for MCV and MCHC. Shareef, 2012 and Shafee, 2016, (15,30) also had similar findings in their works on tuberculosis infection. Other research reports reveals that after anti-tuberculosis therapy (DOTS) with these three combination of drugs, streptomycin, rifampicin and isoniazid, the red cell indices MCV, MCH and MCHC were positively affected and reached close to normal values. RBC morphology in pulmonary TB patients is also seen to be generally normocytic normochromic type and during medication, the blood film showed normochromic pictures (31,32,33). This suggests the positive effects of tuberculosis therapy on the restoration of RBC morphology.

CONCLUSION:

The hematological parameters under study in female Tuberculosis patients at the end of their treatment (DOTS chemotherapy) were not significantly different from those of the control group (i.e. the value of the control compared with that of the second line treatment) except for three parameters (ESR, MCV and MCHC). While our study showed that TB disease significantly affected all the parameters, there was a real improvement in the treatment stage as all parameters were returning back to normal values. This suggests that as time progresses total normalization can occur in all parameters. It is inferred from this that the DOTS chemotherapy has no negative effect on the hematopoietic process. We therefore suggest further studies that will look into the plasma components of patients undergoing DOTS chemotherapy.

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