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Research Article

Haematological Abnormalities in Treatment Naive Multidrug-Resistant Tuberculosis Patients with or Without Human Immunodeficiency Virus (HIV) Infection

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Abstract
Presently, there is the dearth of information on the impact of human immunodeficiency virus (HIV) infection on haematological parameters in patients with multidrug resistant tuberculosis (MDR-TB). Therefore, this study was carried out to determine the levels of selected haematological parameters in MDR-TB patients with or without HIV co-infection before the commencement of MDR-TB therapy. Complete blood count and erythrocyte sedimentation rate (ESR) were determined using an automated haematology analyzer and Westergreen method respectively in 115 patients with MDR-TB. Statistical analysis was done using the Student's t-test, Mann Whitney *U* and Chi square as appropriate. *P*-values less than 0.05 were considered as statistically significant. Twenty-two (19.13%) of the recruited patients had co-infection with HIV. The mean levels of mean corpuscular volume (MCV) and haemoglobin (Hb) were significantly lower in MDR-TB patients compared with patients with MDR-TB/HIV co-infection. The proportion of patients with below reference range (BRR) MCV and mean cell haemoglobin (MCH) was 65% and 73.9% respectively. Similarly, the proportion of patients with BRR haemoglobin (Hb) level was 87% in the two groups with a higher proportion recorded in MDR-TB (90.3%) compared to MDR-TB/HIV co-infection. Also, BRR red cell distribution width (RDW) was recorded in majority (70.4%) of the patients with MDR-TB group having an insignificantly higher proportion (71.0%) compared to MDR-TB co-infection group (68.2%). Treatment naïve patients with MDR-TB have worse CBC findings consistent with iron deficiency anaemia. Hence, assessing haematological parameters before the commencement of MDR-TBtherapy might help in identifying patients that will require appropriate clinical intervention.

Keyword: *Anaemia, Complete blood count, Haematological abnormalities, HIV, Multidrug-resistant tuberculosis*

*INTRODUCTION

Multidrug-resistant tuberculosis (MDR-TB) continues to be a global threat to tuberculosis (TB) control and remains a significant cause of morbidity and mortality especially, in the developing countries (Meressa *et al*., 2015). It was previously considered uncommon in endemic areas of human immunodeficiency virus (HIV) but reports have shown that there has been a 3-4 fold increase in MDR-TB prevalence among people living with HIV in the past decade (Wright *et al*., 2009; Heysell *et al*., 2010). Worldwide, about one fourth of all HIV-related deaths has been attributed to TB co-infection (WHO, 2009; Apidechkul, 2016). Also, Meressa *et al*. (2015) reported that fewer than half of patients with MDR-TB are successfully treated and that poor outcomes are common in HIV-co-infected patients. This indicates that co-infection with MDR-TB and HIV increases morbidity and mortality associated with each of the disease.

Haematological abnormalities are common manifestations of HIV infection (Munyazesa *et al*., 2012). Anaemia and neutropenia have been reported to be the most common haematological abnormalities in HIV (Olaniyi and Aken'Ova, 2003a; Ajayi *et al*., 2009; Akinbami *et al*., 2010). These abnormalities occur as a result of insufficient blood cell production due to bone marrow suppression as a result of HIV infection facilitated by abnormal cytokine expression and alteration of the bone marrow microenviroment (Aboulafia and Mitsuyasu, 1991; Obirikorang and Yeboah, 2009).

Similarly, haematological abnormalities have been reported in patients with tuberculosis (TB) (Al-Omar *et al*., 2009). Olaniyi and Aken'Ova (2003b) and Awodu *et al*. (2007) reported that anaemia, iron deficiency and leukocytosis are common features of TB. The precise mechanism of anaemia in TB is still poorly understood, however, it has been attributed to iron deficiency and cytokines production as a result of inflammation (Ebrahim *et al*., 1995; Lee *et al*., 2006).

Although the pathophysiology of HIV and TB are different, haematologic abnormalities are common to both. Presently, there is little information on the impact of HIV infection on the haematological alterations in patients with MDR-TB before the commencement of MDR-TB therapy. Availability of such information will enable a holistic management as it would facilitate appropriate clinical intervention in addition to the regular MDR-TB regimen. Therefore, this study was

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carried out to determine the complete blood count (CBC) and ESR in treatment naive MDR-TB patients with or without HIV co-infection.

METHODOLOGY

Subjects: Information on the study participants as well as their anthropometric indices have earlier been reported (Ige *et al*., 2016). Briefly, all the MDR-TB patients referred to the MDR-TB Referral Centre, University College Hospital, Ibadan, Nigeria between July 2010 and December 2014 were enrolled into this cross-sectional study. The total number of patients referred within the period was 115 with 22 (19.13%) of them having MDR-TB with HIV co-infection.

Sample collection and laboratory analysis: The determination of complete blood count (CBC) and ESR are part of the pre-treatment medical assessments usually carried out on patients referred to the MDR-TB Unit of the hospital.

Determination of CBC: Five milliliter of venous blood was obtained from each participant and dispensed into EDTA and ESR bottle as required. Haemoglobin concentration (Hb), packed cell volume (PCV), Red cell indices including Mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), red cell distribution width (RDW); total and differential white blood cell count and platelet count along with mean platelet volume (MPV) were determined from the EDTA sample using Swelab alfa 3 part haematology analyzer (9version 2.1, series no SE12613, Boule medicals AB, Sweden).

Determination of ESR: Venous blood sample was collected into citrate bottles containing 3.8% trisodium citrate solution at ratio 1:4 of anticoagulant to blood (4 volumes of blood added to 1 volume of citrate solution). Immediately, this was thoroughly mixed and ESR was determined using Westergreen method.

Statistical analysis

The distribution of all the variables was assessed using histogram with normal curve. Thereafter, differences of variables between groups were assessed using the Student's t-test, Mann Whitney *U* and Fisher's exact test. Results are presented as mean ± standard deviation or median (interquartile range). *P* values less than 0.05 were considered as statistically significant.

RESULTS

As shown in Table 1, the mean PCV and Hb were below normal range in both MDR-TB and MDR-TB/HIV groups. While the PCV was insignificantly lower, the Hb was significantly lower in patients with MDR-TB than in patients with MDR-TB/HIV co-infection. Also, the Mean Cell volume (MCV) and mean cell haemoglobin (MCH) were below normal range in both groups. The mean MCV was significantly lower while the mean MCH was insignificantly lower in patients with MDR-TB compared with patients with MDR-TB/HIV co-infection. The mean level of mean cell haemoglobin concentration (MCHC) was only slightly lower than normal range and no significant difference exists between the two study groups.

The mean total white blood count (WBC) for both groups was within the normal range and there was no significant difference between the 2 groups. In addition, the white cell differentials i.e. Neutrophils, Eosinophils, monocytes, basophils were within the normal reference ranges and in each of the cell types, no significant difference exists between the MDR-TB group and MDR-TB/HIV group. However, the lymphocyte differential count was insignificantly higher in MDR-TB group than MDR-TB/HIV group.

Table 1:
Selected haematological parameters and erythrocyte sedimentation rate in MDR-TB patients and patients with MDR-TB/HIV co-infection

	MDR-TB (n = 93)	**MDR-TB/HIV co-infection (n = 22)**	***P*-values**
TWBC (cells/dl)	9042.42 ± 3567.83	9404.55 ± 3266.64	0.665
RBC (x10)	4.22 ± 0.91	4.01 ± 0.76	0.302
MCV (fL)	70.61 ± 10.75	76.14 ± 7.57	0.025*
MCH (pg)	24.65 ± 5.80	25.02 ± 3.00	0.773
MCHC (g/dl)	30.99 ± 4.66	32.22 ± 1.59	0.227
RDW	15.78 ± 3.59	15.38 ± 4.33	0.652
MPV	10.82 ± 1.17	15.38 ± 4.33	0.661
Hb (g/dl)	9.72 ± 2.11	11.05 ± 1.96	0.009*
PCV (%)	30.61 ± 6.33	32.95 ± 6.49	0.123
Neutrophil (cells/dl)	63.64 ± 13.16	66.86 ± 9.14	0.280
Eosinophil (cells/dl)	2.54 ± 1.21	2.43 ± 1.83	0.737
Monocyte (cells/dl)	4.35 ± 1.71	4.93 ± 1.42	0.108
Basophil (cells/dl)	0.73 (0.00 – 1.00)	1.00 (0.25 – 1.00)	0.063
Lymphocyte (cells/dl)	29.00 (21.00 – 35.00)	25.50 (18.25 – 33.00)	0.261
Platelet ($x10^3$)	325.50 (218.50 – 410.25)	328.00 (202.00 – 399.00)	0.834
ESR ($mm/1^{st}$ hr)	51.00 (28.25 – 85.75)	39.00 (9.00 – 67.00)	0.112

*Significant at *P*<0.05, TWBC=total white blood cell count, RBC=red blood cell count, MCV=, MCH=, MCHC=, RDW=, MPV=, Hb=haemoglobin count, PCV=packed cell volume, ESR=erythrocyte sedimentation rate

Table 2:
Association of MDR-TB/HIV co-infection with selected haematological indices of anaemia

	HIV				
	Yes	**No**	**N**	**X^2**	**P-value**
RBC					
Below reference range	8 (33.30%)	24 (66.70%)	32	1.560	0.458
Within reference range	14 (19.80%)	66 (80.20%)	80		
Above reference range	0 (0.00%)	3 (85.70%)	3		
MCV					
Below reference range	7 (31.8%)	69 (74.2%)	76	16.270	0.000*
Within reference range	15 (68.2%)	22 (23.7%)	37		
Above reference range	0 (0.0%)	2 (2.2%)	2		
MCH					
Below reference range	16 (72.7%)	69 (74.2%)	85	1.959	0.376
Within reference range	6 (27.3%)	18 (19.4%)	24		
Above reference range	0 (0.0%)	6 (6.5%)	6		
MCHC					
Below reference range	0 (0.0%)	14 (15.1%)	14	4.321	0.115
Within reference range	20 (90.9%)	75 (80.6%)	95		
Above reference range	2 (9.1%)	4 (4.3%)	6		
RDW					
Below reference range	3 (13.6%)	3 (3.2%)	6	4.140	0.126
Within reference range	4 (18.2%)	24 (25.8%)	28		
Above reference range	15 (68.2%)	66 (71.0%)	81		
MPV					
Below reference range	1 (4.5%)	1 (1.1%)	2	1.255	0.534
Within reference range	19 (86.4%)	83 (89.2%)	102		
Above reference range	2 (9.1%)	9 (9.7%)	11		
Hb					
Below reference range	16 (72.7%)	84 (90.3%)	100	4.856	0.039*
Within reference range	6 (27.3%)	9 (9.7%)	15		
Above reference range	0 (0.0%)	0 (0.0%)	0		
PCV					
Below reference range	75 (80.6%)	14 (63.6%)	89	2.942	0.096
Within reference range	18 (19.4%)	8 (36.4%)	26		
Above reference range	0 (0.0%)	0 (0.0%)	0		

As shown in Table 2, below reference range (BRR) red blood cell count (RBC), indicative of anaemia, was found in 32 (27.8%) patients. However, the proportion with BRR RBC was insignificantly higher in MDR-TB group (66.7%) than MDR-TB/HIV group (33.3%). BRR haemoglobin (Hb), which is indicative of anaemia, was recorded in 100 (87%) patients but the proportion was significantly higher in the MDR-TB (90.3%) compared to MDR-TB/HIV (72.7%).

Also, the proportion of patients with BRR MCV and MCH was 65% and 73.9% respectively. However, while the proportion with BRR MCV was significantly higher in MDR-TB group (74.2%) than MDR-TB/HIV group (31.8%), the proportion having BRR MCH was insignificantly higher in MDR-TB (74.2%) than MDR-TB/HIV group (72.7%). As regards MCHC, majority of the patients (82.6%) have values within reference range (WRR) with an insignificantly lower proportion in MDR-TB (80.6%) compared with MDR-TB/HIV group (90.9%).

Majority of the patients (70.4%) have above reference range (ARR) red cell distribution width (RDW) but the MDR-TB group have insignificantly higher proportion of 71.0% compared to 68.2% in MDR-TB/HIV group.

In addition, majority of the patients (88.7%) have mean platelet volume (MPV) within reference range (WRR) with almost equal proportion in the 2 groups (86.4% in MDR-TB/HIV group and 89.2% in MDR TB group).

As shown in Table 3, the proportion of patients with neutropenia and basopaenia was insignificantly higher in MDR-TB patients compared with patients with MDR-TB/HIV co-infection. In contrast, the proportion of patients with monocytopaenia and lymphopaenia was insignificantly higher in MDR-TB/HIV co-infection group compared with MDR-TB group. However, monocytosis and lymphocytosis were rare findings in both groups. Although the proportion of patients with thrombocytosis was similar in the two groups, proportion of patients with thrombocytopaenia was insignificantly higher in MDR-TB patients compared with patients with MDR-TB/HIV co-infection.

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Table 3:
Association of MDR-TB/HIV co-infection with platelet, erythrocyte sedimentation rate and selected haematological parameters

	HIV				
	Yes	**No**	**N**	**X^2**	**P-value**
WBC					
Below reference range	1 (4.5%)	2 (2.2%)	3	0.975	0.614
Within reference range	15 (68.2%)	72 (77.4%)	87		
Above reference range	6 (27.3%)	19 (20.4%)	25		
Neutrophil					
Below reference range	0 (0.0%)	2 (2.2%)	2	1.863	0.394
Within reference range	16 (72.7%)	76 (81.7%)	92		
Above reference range	6 (27.3%)	15 (16.1%)	21		
Eosinophil					
Below reference range	0 (0.0%)	0 (0.0%)	0	4.499	0.093
Within reference range	20 (90.9%)	92 (98.9%)	112		
Above reference range	2 (9.1%)	1 (1.1%)	3		
Monocyte					
Below reference range	1 (4.5%)	2 (2.2%)	3	0.402	0.474
Within reference range	21 (95.5%)	91 (97.8%)	112		
Above reference range	0 (0.0%)	0 (0.0%)	0		
Basophil					
Below reference range	5 (22.7%)	45 (48.4%)	50	5.216	0.074
Within reference range	17 (77.3%)	47 (50.5%)	64		
Above reference range	0 (0.0%)	1 (1.1%)	1		
Lymphocyte					
Below reference range	8 (36.4%)	21 (22.6%)	29	2.325	0.313
Within reference range	14 (63.6%)	69 (74.2%)	83		
Above reference range	0 (0.0%)	3 (3.2%)	3		
Platelet					
Below reference range	0 (0.0%)	7 (7.5%)	7	1.840	0.398
Within reference range	16 (72.7%)	60 (64.5%)	76		
Above reference range	6 (27.3%)	26 (28.0%)	32		
ESR					
Below reference range	0 (0.0%)	0 (0.0%)	0	1.283	0.270
Within reference range	4 (18.2%)	9 (9.7%)	13		
Above reference range	18 (81.8%)	84 (90.3%)	102		

DISCUSSION

Tuberculosis infection has significant effect on haemopoiesis and the knowledge of the varying range of haematological alteration can heighten the index of suspicion on suspected patients with tuberculosis. The inherent variability in haematological parameters is usually as a result of complex interplay of factors including host mediated immunity which is expectedly depressed in HIV infection, virulence of invading bacilli and presence or absence of co-morbidities.

Alteration in haematological profile (CBC and ESR) have been reported as a common feature of both HIV and TB (Amilo *et al*., 2013). The main component of red blood cell is Hb, it transports oxygen and carbon dioxide in the blood (Merrit and Curry, 2014a). The observed lower Hb level in MDR-TB patients compared with patients with MDR-TB/HIV co-infection contradicts the report of Amilo *et al*. (2013) who reported that patients with pulmonary TB had similar Hb level as patients with PTB/HIV co-infection. This discrepancy could be as a result of difference in the status of the TB patients studied as our study was centered on patients with MDR-TB whereas their patients had drug sensitive PTB. Our observed lower Hb level probably indicates that anaemia in MDR-TB patients is higher than in patients with MDR-TB/HIV co-infection.

Although Hb level is clinically used to determine the presence of anaemia (Means and Glader, 2009), other haematological factors such as MCV guides in determining the type of the anaemia. In this study, MCV level was significantly lower in MDR-TB patients compared with patients with MDR-TB/HIV co-infection. This observation indicates that the MDR-TB patients probably have microcytic anaemia which could be as a result of iron-deficiency anaemia or anaemia of chronic disorders (Merrit and Curry, 2014b). However, our observation in this study points towards iron-deficiency anaemia as RDW was also slightly higher in MDR-TB patients compared with patients with MDR-TB/HIV co-infection.

Mild lymphocytosis has been reported in TB patients with or without HIV co-infection (Bozóky *et al*., 1997). In this study, lymphocyte and neutrophil counts were not significantly different between the 2 groups. This observation supports the report of Amilo *et al*. (2013). Our observation could indicate that there is similar alteration pattern in lymphocyte and neutrophil counts in MDR-TB patients and patients with MDR-TB/HIV co-infection.

The proportion of patients with Hb and MCV levels within the reference interval was higher in MDR-TB patients with HIV co-infection than MDR-TB patients only. This observation further supports the observed lower mean levels of Hb and MCV in patients with MDR-TB compared with patients with HIV co-infection. Our observed seemingly low alteration in haematological factors in patients with HIV co-infection compared with patients with MDR-TB only could be as a result of anti-retroviral therapy use which would probably prevent profound haematological alteration.

Non-determination of serum ferritin level and inability to recruit antiretroviral-naïve patients with MDR-TB/HIV co-infection are some of the limitations in this study.

It could be concluded from this study that anaemia is common in the patients but appears to be worse in patients with MDR-TB than the patients with MDR-TB/HIV co-infection before commencement of MDR-TB therapy. Also, the red cells indices profile was in keeping with hypochromic-microcytic anemia which appeared more pronounced in MDR-TB group than MDR-TB/HIV group. This indicates that assessing haematological factors before the commencement of MDR-TB therapy might help in identifying patients that will require appropriate clinical intervention.

REFERENCES

Aboulafia, D.M., and R.T. Mitsuyasu. 1991. Hematologic abnormalities in AIDS. Hematol Oncol Clin North Am. 5(2):195-214.

Ajayi, A.O., E.A. Ajayi, and K.A. Fasakin. 2009. CD4+ T-lymphocytes cell counts in adults with human immunodeficiency virus infection at the medical department of a tertiary health institution in Nigeria. Ann Afr Med. 8(4):257-260.

Akinbami A., O. Oshinaike, T. Adeyemo, A. Adediran, O. Dosunmu, M. Dada, I. Durojaiye, A. Adebola, and O. Vincent. 2010. Hematologic Abnormalities in Treatment-Naïve HIV Patients. *Infectious Diseases: Research and Treatment* 3: 45–49.

Apidechkul, T. 2016. A 20-year retrospective cohort study of TB infection among the Hill-tribe HIV/AIDS populations, Thailand. BMC Infect Dis. 16(1):72.

Awodu, O.A., I.O. Ajavi and A.A. Famodu. 2007. Hemorheological variables in Nigeria pulmonary tuberculosis patients undergoing therapy. *Clin. Hemorheol. Microcircula* 36: 267-275.

Bozóky, G., E. Ruby, I. Góhér, J. Tóth and A. Mohos. 1997. Hematologic abnormalities in pulmonary tuberculosis. *Orv Hetil.* 138(17):1053–1056.

Ebrahim, O., P.I. Folb and J.P. Robson. 1995. Blunted erythropoietin response to anemia in tuberculosis. *Eur. J. Hematol*. 55: 251-254.

Amilo, G.I., S. C. Meludu, P. U. Ele, C. Ezechukwu, C. Onyenekwe, and M. Ifeanyi Chukwu. 2013. Hematologic Indices in Pulmonary Tuberculosis with or without HV Co-Infection in South Eastern Nigeria. *Advances in Life Science and Technology* 11:1-7.

Heysell, S.K., T.A. Thomas, N.R. Gandhi, A.P. Moll, F.J. Eksteen, Y. Coovadia, L. Roux, P. Babaria, U. Lalloo, G. Friedland and S. Shah. 2010. Blood cultures for the diagnosis of multidrug-resistant and extensively drug-resistant tuberculosis among HIV-infected patients from rural South Africa: a cross-sectional study. BMC Infect Dis. 10:344.

Al-Omar, I.A., R.M. Al-Ashban and A.H. Shah. 2009. Hematological Abnormalities in Saudis Suffering from Pulmonary Tuberculosis and Their Response to the Treatment. *Research Journal of Pharmacology* 3(4): 78-85.

Ige, O., K. Akinlade, S. Rahamon, V. Edem and O. Arinola. 2016. Thyroid function in multidrug-resistant tuberculosis patients with or without human immunodeficiency virus (HIV) infection before commencement of MDR-TB drug regimen. *African Health Sciences 16(2):* 596-602

Lee, S.W., Y.A. Kang, Y.S. Yoon, S.W. Um, S.M. Lee, C.G. Yoo, Y.W. Kim, S.K. Han, Y.S. Shim and J.J. Yim. 2006. The prevalence and evolution of anemia associated with tuberculosis. *J Korean Med Sci.* 21(6):1028-1032.

Means, R.T., and B. Glader. 2009. Disorders of Red Cells. Greer JP, Foester J, Rodgers GM, et al, eds. Wintrobe's Clinical Hematology. 12th ed. Philadelphia, PA: Lippincott Williams & Wilkins; Chapter 26.

Meressa, D., R.M. Hurtado, J.R. Andrews, E. Diro, K. Abato, T. Daniel, P. Prasad, R. Prasad, B. Fekade, Y. Tedla, H. Yusuf, M. Tadesse, D. Tefera, A. Ashenafi, G. Desta, G. Aderaye, K. Olson, S. Thim and A.E. Goldfeld. 2015. Achieving high treatment success for multidrug-resistant TB in Africa: initiation and scale-up of MDR TB care in Ethiopia-an observational cohort study. Thorax 70(12):1181-1188.

Merritt, B.Y., and C.V. Curry. 2014a. Hemoglobin Concentration (Hb). Available: http://emedicine.medscape.com/article/2085614-overview#a2, Accessed on May 6, 2016.

Merritt, B.Y., and C.V. Curry. 2014b. Mean Corpuscular Hemoglobin (MCH) and Mean Corpuscular Hemoglobin Concentration (MCHC). Available: http://emedicine.medscape.com/article/2054497-overview, Accessed on May 6, 2016.

Munyazesa, E., I. Emile, E. Mutimura, D.R. Hoover, Q. Shi, A.P. McGinn, S. Musiime, F. Muhairwe, A. Rutagengwa, J.C. Dusingize, K. Anastos. 2012. Assessment of haematological parameters in HIV-infected and uninfected Rwandan women: a cross-sectional study. BMJ Open. 2(6).

Obirikorang, C., and Yeboah, F.A. 2009. Blood hemoglobin measurements as a predictive indicator for the progression of HIV/AIDS in resource-limited setting. *J Biomed Sci* 16:102.

Olaniyi, J.A., and Y.A. Aken'Ova. 2003a. Bone marrow findings in patients with pulmonary tuberculosis. *Afr J Med Med Sci.*. 32(2): 155-157.

Olaniyi, J.A., and Y.A. Aken'Ova. 2003b. Haematological profile of patients with pulmonary tuberculosis in Ibadan, Nigeria. *Afr J Med Med Sci.* 32(3):239–242.

World Health Organization. 2009. Global tuberculosis control: epidemiology, planning, financing: WHO report. Geneva.

Wright, A., M. Zignol, A. Van Deun, D. Falzon, S.R. Gerdes, K. Feldman, S. Hoffner, F. Drobniewski, L. Barrera, D. van Soolingen, F. Boulabhal, C.N. Paramasivan, K.M. Kam, S. Mitarai, P. Nunn, M. Raviglione; Global Project on Anti-Tuberculosis Drug Resistance Surveillance. 2009. Epidemiology of antituberculosis drug resistance 2002-07: an updated analysis of the Global Project on Anti-Tuberculosis Drug Resistance Surveillance. Lancet. 373(9678):1861-1873.

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