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Orapuh Journal

ORIGINAL ARTICLE

Journal of Oral & Public Health

Haematological disorders in tuberculosis at the Monkole Referral Hospital (Kinshasa, Democratic Republic of the Congo): A case report of 50 patients

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ARTICLE INFO

Received: *06 January 2024*
Accepted: *29 January 2024*
Published: *16 February 2024*

Keywords:
Tuberculosis, Haematological disorders, haemogram, Monkole Hospital, Democratic Republic of the Congo

Peer-Review: *Externally peer-reviewed*

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To cite:
Bolisomi, S. B., Basilua, J. K. , Iyombe, J. E., Mawunu, M., Masengo, C. A., Inkoto, C. L., & Ngbolua, K. N. (2024). Haematological disorders in tuberculosis at the Monkole Referral Hospital (Kinshasa, Democratic Republic of the Congo): A case report of 50 patients. *Orapuh Journal*, 5(1), e1107. https://dx.doi.org/10.4314/orapj.v5i1.7

ISSN: *2644-3740*

Published by Orapuh, Inc. (info@orapuh.org)

Editor-in-Chief: Prof. V. E. Adamu
Engelhardt School of Global Health & Bioethics, Euclid University (Pôle Universitaire Euclide) – www.euclid.int

ABSTRACT

Introduction

Tuberculosis is an infectious disease that affects people around the world and is a major public health problem, with TB transmitted by humans and air. Some of the haematological disorders that are associated with tuberculosis are anemia, leukemia, and/or lymphopenia

Purpose

This study aimed to investigate hematological disorders in patients with tuberculosis.

Methods

This study was conducted at Monkole Hospital (Kinshasa, Democratic Republic of the Congo). A total of 50 tuberculosis patients were included in this case study. Blood samples were collected and analyzed to assess hematological parameters. Patients were randomly selected, and demographic data were gathered for in-depth analysis.

Results

The analysis revealed that anaemia was the sole hematological disorder observed in tuberculosis patients, with an average hemoglobin level of 8.6 g/dl. Examining erythrocyte indices, the predominant types of anaemia were normochromic normocytic anaemia and hypochromic normocytic anaemia.

Conclusion

This study confirmed that anaemia and leukopenia are common hematological disorders in patients with tuberculosis. The results of this study can have significant implications for the clinical management of tuberculosis patients. By gaining a better understanding of hematological disorders associated with tuberculosis, healthcare professionals can tailor their diagnostic and therapeutic approaches to enhance the quality of care provided to tuberculosis patients. This information can also guide future research into the hematological complications of tuberculosis, contributing to the development of more effective treatment strategies.

INTRODUCTION

Context and definition of the problem

Tuberculosis is an infectious disease that affects people around the world and is a major public health problem, with TB transmitted by humans and air (Toujani, 2015). Human tuberculosis is mainly caused by a limited number of variants of *Mycobacterium* (MTBC) called *Mycobacterium tuberculosis* complex, the most important of which is BK (Bacillus Koch). The latter causes the majority of human tuberculosis cases. More than one-third of the world's population is infected with BK. Humans are still the main natural reservoirs of *M. tuberculosis*, but the disease also affects many animals. The lung is the most common source of BK infection, both an entrance point for tuberculosis bacteria and an organ that is chosen for disease development. Pulmonary tuberculosis is the only form of infectious disease (Kouloud, 2022).

According to the World Health Organization (WHO) World TB Report 2022, TB has caused about 10.6 million deaths in 2021, an increase of 4.5% from 2020, and 1.6 million deaths (including 187,000 HIV-positives). The burden of drug-resistant tuberculosis increased by 3% between 2020 and 2021, and in 2021 450,000 new cases of HIV-resistant tuberculosis (WHO, 2022). In Africa, the mortality rate is estimated at 81 deaths per 100,000 people, the highest in the world (Amadou et al., 2019). The Democratic Republic of the Congo (DRC) is one of the 22 countries in the world that are the most affected, at fifth place in Africa and 11th place in the world. In the Democratic Republic of the Congo, the incidence of microscopy-positive pulmonary tuberculosis (TB) is estimated to be 160 per 100,000 people (Amadou et al., 2019).

Early diagnosis of affected persons is an important factor in limiting tuberculosis transmission and thus fighting the disease. Tuberculosis is diagnosed by testing the causes of the bacterial infection in the sample (microscope examination, culture, or gene amplification test). Other tests, such as X-rays and scans, show cancer-causing damage (Kouloud, 2022). Millions of people are diagnosed with tuberculosis each year, but there are still large differences between the expected cases and the notifications. The appropriate treatment of patients is one of the main thrusts of the control of tuberculosis. Since 1950, the treatment of this epidemic has included the combination of several molecules, especially Riflucine (RIF), Isoazid (INH), Ethambutol (EMB), and Pza. However, over time, bacteria that cause the disease developed drug-resistant tuberculosis (DR-TB) which included three major entities. These are rifampicin-resistant tuberculosis (RR-TB), multidrug-resistant tuberculosis (MDR-TB), and XDR-TB (Amadou et al., 2019). In addition, haematological disorders of tuberculosis, such as anemia, leukemia, and/or lymphopenia (Amadou et al., 2019), are frequent. To our knowledge, many studies have not examined hemorrhagic disorders in tuberculosis. Therefore, the study aims to answer the question of what haematological disorders exist in tuberculosis. This study aims to identify hematological disorders of tuberculosis.

METHODS

Study area and period

This study was carried out in the provincial city of Kinshasa. Samples were taken and analysed at Monkole Hospital during the period 11 May to 11 August 2023.

Study population and sample selection

The research sample comprised individuals both with and without tuberculosis. Tuberculosis patients were chosen through a random sampling method

Biological material

The biological material used consisted of whole blood collected in EDTA tubes from tuberculosis patients treated at the Monkole Hospital, Kinshasa.

Equipment and laboratory reagents

A diverse array of equipment and chemical reagents were utilized, including Automated Sysmex XN1000; gloves; semi-automatic tourniquet; syringes; tubes with EDTA; rack; cotton wool; vacuum needle; vacuum body; denatured alcohol; isothermal tray; marker; Cellpack DCL, Cellpack DFL; Cellclean Auto; Sulfolyser SLS; Lysercell WNR; Lysercell WDF; Fluorocell WNR; Fluorocell WDF, and Fluorocell RET.

Selection criteria

- *Inclusion criteria*

  All tuberculosis patients who were admitted to Monkole Referral Hospital for treatment during the study period who consent to be included in the study;

all new suspected tuberculosis patients who were not treated; all tuberculosis patients who had not been treated; all patients who were not treated; all patients who had been selected near the case and who had all the characteristics of the latter except tuberculosis cases.

- *Exclusion criteria*
  Furthermore, all subjects that did not meet the above inclusion criteria were excluded from the study.

Type and duration of the study

This was a prospective, analytical case-control study. It was held at the Monkole Referral Hospital in Kinshasa, Mont Ngafulu.

Analysis method

The samples were collected from tuberculosis patients (first group) and non-tuberculosis patients (second group). On average, 5 ml of complete blood collected in anticoagulants (EDTA) was analysed with the Sysmex XN-1000 hemoglobin analyzer.

Automaton principle

Blood count analyzers employ various technologies. When blood samples with an anticoagulant (EDTA) are introduced into the analyzer, the blood undergoes aliquoting (separation into small portions before being used in different channels) and is treated with different reagents to unveil the specific properties of the cells. Red blood cells and platelets are concurrently measured at a counting port using the impedance technique combined with hydrodynamic focusing. A cyanide-free reagent is utilized for photometrically measuring hemoglobin. Flow fluorocytometry serves as the primary detection method for leukocyte count, reticulocyte count, and erythroblast count. The complete blood count (haemogram) is obtained by drawing a blood sample into a tube containing EDTA as an anticoagulant, typically from the elbow crease. The collected blood sample must be thoroughly mixed, free from clots, and non-hemolytic. Fasting is not a requirement for the patient.

Quality control

Quality control is the regular monitoring of performance through commercial or patient controls. Controls with known characteristics are analyzed and compared to known reference values using statistical methods. This allows you to detect performance changes and act if they are significant or deviate from the Levey-Jennings curve.

- *Frequency*
  Quality control can monitor the performance of the instrument over time. XN CHECK is a quality control tool for monitoring the performance of XN analyzers. Quality control must always be carried out every day in accordance with the regulations of professional regulatory bodies. Please note that additional checks may be required to eliminate all errors.

- *Performing a QC analysis*
  To perform a body fluid analysis quality control or other quality control using an external quality control sample or a remaining sample, perform a manual analysis as described below:

  i. Check that the Status Indicator LED is not lit green, wait until it is;
  ii. If the tube holder has not been ejected, press the Mode button. The tube holder will be ejected;
  iii. Click on the change analysis mode button in the control menu. A dialogue box will appear, select the "whole blood" mode;
  iv. Click on "OK" and the dialogue box will close;
  v. Click on the Analyser menu button in the control menu. The menu shown opposite will appear;
  vi. Click on "QC Analysis" and a dialog box will appear with a list of QC files.
  vii. In the list of QC files, click on the file you wish to analyse. The dialog box shown opposite will appear;
  viii. Analyse the controls manually;
  ix. Check the analysis results. At the end of the analysis, the results are displayed in the <Execute L-J> dialog box.

Analysis methods

You can select the analysis mode for different samples.

A. Mode (Whole Blood), used for whole blood analysis
B. Mode (Low WBC), used for low WBC analysis with whole blood.
C. Mode (Pre-dilution), used to analyse a minute amount of blood from the earlobe or fingertip.

D. Mode (Liq punct), used to analyse puncture fluids (CSF, synovial fluid, peritoneum, and pleura).
E. Mode (HPC), used to analyse HPC-related parameters using whole blood.

Manual analysis process

I. Check the Status Indicator LED on the analyser if it is green.
II. If the tube holder has not been ejected, press the Mode button. The tube holder will be ejected.
III. Click on the Change measurement mode button in the control menu. The dialog box shown opposite will appear and specify the analysis mode to be performed:
   - Whole blood
   - Low WBC
   - Pre-dilution
IV. Click on "OK" to close the dialog box.
V. Click on the Ana manual button in the control menu. A dialogue box corresponding to the selected mode will appear.
VI. Click on "OK" to close the dialog box.
VII. Shake the sample tube vigorously as indicated.
VIII. Place the sample tube on the sample tube holder. There are two sample tube holders, for the normal tube and the micro tube. When placing a micro-sample tube, insert it securely so that the bottom of the tube touches the base of the holder.
IX. Press the START button on the analyser. The tube holder slides into the unit and sample aspiration begins. At the end of the analysis, the tube holder will be ejected.
X. Remove the sample. To analyse another sample, repeat steps 3 to 10.

Table 1:
Expression of results

Parameters	3 à 10 years	Female	Male
Red blood cells (million/mm³)	4.0-5.4	4.0 - 5.3	4.2 - 5.7
Haemoglobin (g/100ml)	12.0 - 14.5	12.5 - 15.5	14.0 - 17.0
Hematocrit (%)	36 - 45	37 - 46	40 - 52
MCV (µ³)	74 - 91	80 - 95	80 - 95
MCHR (pg)	24 - 27	28 - 32	28 - 32
MCHC (%)	28 - 33	30 - 35	30 - 35
Leucocytes (mm³x1000)	5000 - 11000	4000 - 10000	4000 - 10000
Reticulocytes (%)	0.2 - 0.8	0.3 - 0.8	0.3 - 0.8

***Legend**: MCV (Mean Corpuscular Volume); MCHR (Mean Corpuscular Hemoglobin Rate); MCHC (Mean Corpuscular Hemoglobin Concentration)*

Ethical considerations

Samples were collected from individuals, both with and without tuberculosis, who had voluntarily agreed to participate in the study. Ensuring anonymity was imperative to safeguard the well-being and privacy of these individuals.

Data processing

The data were inputted and analyzed using SPSS version 21.0 software. Statistical analysis included calculating the mean age of the study population and assessing frequencies. For the study parameters, specifically the hemogram, comparisons between tuberculosis patients and non-tuberculosis patients were conducted using Welch's 0.05 test. Proportions of different types of anaemia in both groups were compared using Pearson's Chi-square test, with Fisher's exact test applied for smaller sample sizes.

RESULTS

Table 2 shows the distribution of patients by age group.

Table 2:
Breakdown of patients by age group

Age groups (years)		Subjects		Total
		Tuberculous	Non-tuberculous	
17 - 37	Frequency	6	16	22
	%	6.0	16.0	22.0
38 - 58	Frequency	21	26	47
	%	21.0	26.0	47.0
59 - 79	Frequency	23	8	31
	%	23.0	8.0	31.0
Total	Frequency	50	50	100
	%	50.0	50.0	100.0

Table 2 presents details regarding the age distribution of the study participants. Among tuberculosis patients, the predominant age group was 59 to 79 years, accounting for 23 subjects (23%). In contrast, for non-tuberculosis patients, the most prevalent age group was 38 to 58, comprising 26 subjects (26%). The overall mean age across all participants was 50±14 years.

Table 3 shows the distribution of patients by sex compared to those who are non-tuberculous.

Table 3:
Distribution of subjects by sex

Category		Sex		Total
		Male	Female	
TB patients	Frequency	33	17	50
	%	33.0	17.0	50.0
Non- tuberculous	Frequency	22	28	50
	%	22.0	28.0	50.0
Total	Frequency	55	45	100
	%	55.0	45.0	100.0

Table 3 indicates that out of the total 55 patients, 55% were male, with 33% having tuberculosis and 22% being without tuberculosis.

Table 4 compares the mean haemoglobin levels of the patients with those who are non-tuberculous.

Table 4:
Comparison of patients' mean haemoglobin levels

Parameters	Patients	N	Average	SD	p-value
Hemoglobin (g/dl)	Tuberculous	50	8,6	1,5	0,001
	Non-tuberculous	50	11,4	2,4	

***Legend**: Standard deviation (SD)*

Table 4 demonstrates that the average hemoglobin level in patients with tuberculosis was 8.6 ± 1.5 g/dl. In contrast, the mean hemoglobin level in non-tuberculosis patients was 11.4 ± 2.4 g/dl. This difference was statistically significant (p = 0.001).

Table 5 compares the mean hematocrit levels of the examined patients with those who are non-tuberculous.

Table 5:
Comparison of patients' mean haematocrit levels

Parameter	Patients	N	Average	SD	p-value
Hematocrit (%)	Tuberculous	50	26.5	4.6	0.001
	No tuberculous	50	35.9	7.3	

Table 5 indicates that the average hematocrit level among patients with tuberculosis was 26.5 ± 4.6%. In contrast, the second table reveals that the mean hematocrit level was 35.9 ± 7.3%. The difference was statistically significant (p = 0.001).

Table 6 provides the mean red blood cell values for tuberculosis patients compared to non-tuberculous patients.

Table 6:
Comparison of patients' mean red blood cell values

Parameters	Patients	N	Average	SD	p-value
Red cells (10^6/µl)	Tuberculous	50	3.1	1	0.001
	No tuberculous	50	4.3	1	

Table 6 provides the average red blood cell values for the study participants. Among tuberculosis patients, the mean red blood cell count was 3.1 ± 1.106/µl of blood, while in non-tuberculosis patients; the mean value was 4.3 ± 1.10^6/µl of blood.

Table 7 compares the mean white blood cell values of the studied patients with those who are non-tuberculous.

Table 7:
Comparison of patients' mean white blood cell values

Parameter	Patients	N	Average	SD	p-value
White blood cells /µL)	Tuberculous	50	8760	562 1	0.012
	Non-tuberculous	50	6464	278 3	

Table 7 indicates that the average white blood cell count was 8760 ± 5621/µl of blood in tuberculosis patients. In contrast, the mean white blood cell count in non-tuberculosis patients was 6464 ± 2783/µl of blood. This difference was statistically significant (p = 0.012).

Table 8 compares the mean platelet values of the patients studied with those who are non-tuberculous.

Table 8:
Comparison of patients' mean platelet values

Parameter	Patients	N	Average	SD	p-value
Platelets (µL of blood)	Tuberculous	50	263880	122867	0.001
	Non-tuberculous	50	270507	153979	

The data presented in Table 8 indicate that the average platelet count was 263,880 ± 122,867/µl of blood among tuberculosis patients. In contrast, non-tuberculous patients had a mean platelet count of 270,507 ± 153,979/µl of blood. This difference was statistically significant (p = 0.001).

Table 9 compares the mean MCV (Mean Corpuscular Volume) values of the patients studied with those who are non-tuberculous.

Table 9:
Comparison of mean MCV values of patients

Parameter	Patients	N	Average	SD	p-value
MCV (fl)	Tuberculous	50	86	9	0.902
	Non-tuberculous	50	86	28	

Table 9 indicates that the mean corpuscular volume (MCV) value in tuberculosis patients was 86 ± 9 fl. In contrast, this value was 86 ± 28 fl in non-tuberculosis patients. The observed difference was not statistically significant (p = 0.902).

Table 10 compares the mean MCHR (Mean Corpuscular Hemoglobin Rate) values of the patients studied with those who are non-tuberculous.

Table 10:
Comparison of patients' MCHC values

Parameters	Patients	N	Average	SD	p-value
MCHR (pg)	Tuberculous	50	27	3	0.823
	Non-tuberculous	50	27	9	

Table 10 shows that the mean value of MCHR in tuberculosis patients is 27±3 pg. In contrast, in non-tuberculosis patients, this value was 27±9 pg. The difference is not significant (0.823).

Table 11 shows a comparison of the mean values of the MCHC (Mean Corpuscular Hemoglobin Concentration) of the patients studied.

Table 11:
Comparison of mean MCHC values of patients

Parameters	Patients	N	Average	SD	p-value
MCHC (%)	Tuberculous	50	32	2	0.465
	No tuberculous	50	32	3	

Table 11 shows that the average value of MCHC in tuberculosis patients was 32 2%. On the other hand, in non-tuberculous patients, this value was 323%. The difference was not significant (0,465).

Table 12 shows the distribution of patients by type of anaemia.

Table 12:
Distribution of patients by type of anaemia

	Tuberculous		No Tuberculous			
Types of anemia	Yes	No	Yes	No	Test (χ^2)	p-value
AnNN	22	28	13	37	3,560	0,093
AnNH	28	22	13	37	3,560	0,004
AnMaN	1	49	3	47	1,031	0,310
AnMaH	0	50	4	46	4,125	0,042
AnMiN	9	41	8	42	0,071	0,790
AnMiH	2	48	11	39	7,090	0,008
GrMaN	0	50	1	49	1,000	0,317

Legend: (AnNN: Normochromic normocytic anaemia ; AnNH: Hypochromic normocytic anaemia; AnMaN: Macrocytic Normochromic Anemia; AnMiN: Normochromic Microcytic Anemia; AnMiH: Hypochromic Microcytic Anemia; GrMaN: Normochromic Macrocytic Red Blood Cell).

Table 12 shows that in 28 cases, the most common type of anaemia in tuberculosis patients is normal hypochromic anaemia. The second type was normocytic normochromic anaemia with 22 cases. Two types of anaemia are the most common among non-tuberculosis patients. These were normochromic normocytic anaemia and hypochromic normocytic anaemia, each with 13 cases.

DISCUSSION

This study focused on hematological disorders in tuberculosis patients, aiming to address the question of which hematological disorders are prevalent in tuberculosis cases.

Table 2 presents the distribution of age groups among the subjects. The most common age group for tuberculosis patients was 59 to 79 years, comprising 23 subjects (23%). Conversely, for non-tuberculosis patients, the predominant age group was 38 to 58, with 26 subjects (26%). Overall, the mean age across all subjects was 50 ± 14 years. Our findings align closely with those of a study conducted in Niger by Amadou et al. (2019) on the epidemiological, clinical, and evolutionary profile of tuberculosis patients at the Maradi Regional Hospital, Republic of Niger. In that study, the mean age of tuberculosis patients was 42.3 ± 10.1 years, with a range from 13 months to 85 years, confirming the contagious nature of the disease, affecting individuals of all ages based on their exposure (Amadou et al., 2019). This observation was similarly noted by Lubala et al. (2012) in their investigation of the epidemiological and clinical profile of tuberculosis in the Lubumbashi health zone (Democratic Republic of the Congo). Tuberculosis patients registered in a health center of the Lubumbashi health zone had an average age of 33 ± 15 years, with the most affected

age groups falling within the 21-30 years range (Ngama et al., 2014).

About the sex, **Table 3** shows that men's sex is predominant with 55 subjects or 55 percent, including 33 percent of tuberculosis patients and 22 percent of non-tuberculosis patients. This male dominance has been proven in several studies (Ngama et al., 2014). Ngama et al. also showed that men accounted for 70% of the cases and accounted for the majority.

As far as the hemoglobin level is concerned, the average hemoglobin level in the patient is 8.61.5 g/dl, and in **Table 4** on tuberculosis hemoglobin disease is the only hemoglobin disease observed in the patient. There is no doubt that tuberculosis is the cause of this anemia. It is undoubtedly due to one type of hemolytic action, but the intimate mechanism has not yet been revealed. Our results are consistent with those of Moussaoui et al. (2015), who also found that the mean hemoglobin level in tuberculosis patients is 8.9/dl. The table also shows that the average hemoglobin levels in patients without tuberculosis are 11.42.4g/dl. It is believed that anemia in non-tuberculosis patients is caused by other factors. The difference was significant ($p = 0.001$). In the same vein, the data presented in tables 9, 10, and 11, complemented by those in table 12, reveal that the most prevalent types of anemia were as follows: normocytic hypochromic anemia with 28 cases. The second most common type of anemia was normochromic normocytic anemia, documented in 22 cases. Similar findings have been reported in other studies, such as that of Habibi et al. (2017). These two types of anemia were also observed in non-tuberculosis patients. Regarding leukocytes, as depicted in Table 7, the mean white blood cell count was 8760 ± 5621/µl of blood in TB patients. Our results contradict those of some other studies that report hyperleukocytosis (Habibi et al., 2017), while others have indicated leukopenia in TB patients (Moussaoui et al., 2015).

About thrombocytes, the data presented in **Table 8** indicate that the mean platelet value was 263880 ± 122867/µl of blood in TB patients. Conversely, the mean platelet count in non-tuberculous patients was 270507 ± 153979/µl of blood, with a significant difference ($p = 0.001$). The results of this study are consistent with other studies showing thrombocytopenia rare, and few publications mention the thrombocytopenic purpura associated with tuberculosis (Lubala et al., 2012; Azzeddine et al., 2019). Furthermore, the original study used a diagnostic tool, the Sysmex XN-1000 hemodynamic analyzer, to perform hemodynamic investigations with high accuracy and therefore provide reliable results.

Limitations of the study

The present study was limited to the quantitative aspect of the haemogram, and the classification of anaemia was based solely on erythrocyte constants. The white blood cell count was not performed during this study. In the future, we will conduct studies addressing all these outstanding aspects.

CONCLUSION AND RECOMMENDATIONS

This study has highlighted the importance of understanding hematological manifestations in tuberculosis patients. The results obtained from the analysis of 50 cases revealed that two hematological abnormalities are associated with tuberculosis, including anaemia and leukopenia, offering valuable insights for improved clinical management. These findings contribute to the enrichment of knowledge about tuberculosis, paving the way for future research and more targeted therapeutic strategies to enhance clinical outcomes for patients.

The following recommendations are thus formulated:

- The Government, through the National Tuberculosis Control Program, should make drugs available for individuals with tuberculosis, provide nutritional support for tuberculosis patients, and motivate healthcare providers to deliver quality care.
- Tuberculosis patients should adopt a balanced diet to prevent or correct anaemia

Acknowledgment: The authors express their gratitude to Monkole Hospital and the National Tuberculosis Control Program for their assistance in conducting this study.

Ethical Approval: Nil required

Conflicts of Interest: None declared.

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