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Original Research Article

Profile of haematological indices among pulmonary tuberculosis patients attending Kisii teaching and referral hospital, Kenya

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ABSTRACT

Background: Tuberculosis, caused by *Mycobacterium tuberculosis*, affects approximately 10 million people worldwide, with an annual global mortality rate of 1.4 million (WHO, 2021). This study aimed to profile hematological indices among pulmonary tuberculosis patients at Kisii teaching and referral hospital, Kenya from February 2022 to July 2022 where Kisii County reports around 1800 TB cases annually.
Methods: A cross-sectional study design with 210 participants was used, 105 patients and 105 controls. Venous blood was collected in ethylene diamine tetra acetic and analyzed using flow cytometry technique. Erythrocyte sedimentation rate was set by use of Westergren technique while a thin blood film was prepared for microscopic examination of cells. Data obtained was analyzed using Stata version 23.
Results: Female patients accounted for 55 (52.5%) of positive cases while males accounted for 50 (47.5%). PTB patients showed significantly lower RBC count, HGB, HCT, MCH, and MCHC compared to controls (p=0.001). ESR was significantly higher in PTB patients (p=0.001). PTB patients had higher platelet count and total WBC count (p=0.009 and p=0.018, respectively) with increased neutrophil and monocyte counts (p=0.044 and p=0.041, respectively). No significant differences were observed in lymphocyte counts (p=0.086).
Conclusions: The study identified significant hematological abnormalities in pulmonary tuberculosis patients, including normocytic normochromic anemia, toxic granulation in white blood cells, and thrombocytosis, highlighting these as potential diagnostics and clinically significant hematological parameters in the management of pulmonary tuberculosis.

Keywords: Pulmonary tuberculosis, Hematological profile, Hemoglobin level, Thrombocytosis, Kisii teaching and referral hospital

INTRODUCTION

Tuberculosis (TB) is a global public health concern, with a high burden of cases and mortality worldwide. In 2020 alone, there were an estimated 10 million new TB cases and 1.5 million deaths attributed to the disease.[1] TB is caused by the bacterium *Mycobacterium tuberculosis* and primarily affects the lungs, although it can also affect other parts of the body.[2] Transmission occurs through airborne droplets, contaminated food products such as the consumption of unpasteurized milk and meat infected with *M. tuberculii*.[3] Developing countries, particularly in Asia and Africa, bear the brunt of TB epidemic, with high rates of HIV comorbidity, socio-economic challenges, and the emergence of drug-resistant strains contributing to the problem.[2,4]

Kenya is among the countries heavily impacted by TB, with a reported prevalence of 558 cases per 100,000 individuals in 2016.[5] The highest burden of TB cases was observed in the age group of 25-34 years, with urban

areas exhibiting higher rates.[5] However, the prevalence-to-notification ratio of 2.5 to 1, indicates that a significant number of TB cases go undetected and untreated, emphasizing the need for improved screening and diagnostic methods.[6] Kisii County, in particular, has experienced a high prevalence of TB, with 8.4% of cases reported among children.[5]

Early diagnosis and treatment of TB remain challenging due to the disease's nonspecific initial symptoms. Laboratory diagnosis often occurs at an advanced stage, hampering intervention measures.[4] The existing laboratory networks in Kenya face limitations in terms of efficiency, trained healthcare personnel, and adequate equipment. Standard diagnostic methods such as microscopy and culture have their drawbacks in terms of accuracy and time required for results.[6] Therefore, establishing a hematological profile that can serve as a differential diagnosis for TB patients could significantly improve timely management and control of the disease.

This study focuses on investigating the hematological profile among pulmonary TB patients attending Kisii teaching and referral hospital in Kenya. The results will contribute to filling the gap in knowledge regarding hematological indices in TB patients and provide a foundation for more effective diagnostic approaches.

METHODS

Study site

This study was conducted at Kisii teaching and referral hospital (KTRH), Kenya from February 2022 to July 2022.

Research design

A cross-sectional study design was used involving TB patients attending KTRH.

Study population

The population for this study was all TB patients seeking services at the chest clinic at KTRH at the time of study.

Sample size

Yamane's (1967) formulae for sample size calculation was used to calculate the sample size for the participants.

$N=N/1+N(e^2)$

Where; N=population of TB patients at KTRH chest clinic, that is 142 TB patients.

n=desired sample size

e=sampling error at 95% confidence level

The sample size was calculated as follows: $n=142/1+142(0.05)^2 \approx 104.7 \approx 105$ patients.

Sampling technique

Tuberculosis patients who were confirmed to have tuberculosis infection and met the inclusion criteria at KTRH during the study period. The control subjects were selected based on eligibility and matched with the case group to ensure comparability. The recruitment of both patients and control allowed for a comprehensive analysis of the hematological profile among PTB patients and facilitated the comparison of results between the two groups.

Inclusion criteria

Patients who were not on anti-tuberculosis drug, no record of any other chronic disease, non-pregnant women and HIV negative patients were included in the study.

Healthy people of age group 18 years and 70 years were included in the study.

Exclusion criteria

Those who were below 18 years of age and those who were above 70 years; those who were TB negative; and finally, patients who had no signs of concomitant chronic or acute infection other than pulmonary tuberculosis, bleeding manifestations, endocrine disorders, other organ dysfunction or systemic disorders and chronic inflammatory disease on clinical examination were not included as PTB group.

Sample collection

The study participants were assessed and recruited according to the WHO standardized tool adopted to collect samples from confirmed TB patients attending KTRH. Eligible participants were then prepared for venous blood sample collection. A gauge 18 needle was inserted into the vein and the blood was collected in an airtight syringe. Approximately 4 ml of each blood was collected aseptically using the EDTA tube from each of the study participants and the EDTA tube correctly labeled with the patient's identification number.

Blood samples processing and analysis

Venous blood samples collected in EDTA vacutainer tubes were analyzed using the Sysmex XN-330 cell counter, which utilizes flow cytometry. This tested for total white blood cell, total red blood count, differential count for neutrophils, lymphocytes, monocytes, basophils and platelets. The procedure involved mixing the blood sample with the anticoagulant in the tube, measuring leukocytes using absorbance and scattered light at multiple angles to determine cell characteristics, and utilizing internal and external controls for quality

assurance. Differential leukocyte count was obtained using the flow cytometry machine, while erythrocyte sedimentation rate (ESR) was measured by vertically standing blood and observing stained blood films. The technique was simple, utilizing a primed coulter counter machine with programmed software for result generation. A thin blood film was prepared by dropping blood on a microscopic slide, drying and staining with Leishman for observation.

Data analysis

The data obtained was analyzed using Stata version 23 to obtain the mean and p values for the independent samples T test. The independent samples T test was used to determine if there was a statistically significant variation in the hematological profiles between the two groups. The results were presented in tables and figures.

Ethical approval

The study was conducted after receiving the ethical approval from the university of East African, Baraton University ethical committee (UEAB/REC/12/10/2021) and permission was sought from Kisii university, NACOSTI (NACOSTI/P/22/15517) and Kisii teaching and referral hospital. The informed written consent was obtained from the patients who participated in this study. Patients were explained every procedure to be performed and why the test was to be done. Sound ethical reasoning and judgment was necessary in pain management during specimen collection. This included reassuring patient early enough about some pain and assure if pain continues then the patient is advised to come back to hospital. The blood removal place was secure enough to ensure privacy and only one technologist was handling all cases to ensure confidentiality. In order to ensure the respondents' confidentiality, no identity was required.

RESULTS

Demographics

The study comprised 105 confirmed TB patients, consisting of 50 males (47.5%) and 55 females (52.5%). The age range of the participants was between 18 and 70 years, with an average age of 35.41±1.55 years. Notably, the age group with the highest representation was 44-56 years, accounting for 50% of the entire patient population. In contrast, the age groups 18-30 years and 57-69 years constituted 5% and 12.5% of the patient population, respectively.

Regarding marital status, 57.5% of the participants were married, while 37.5% were single. Widows and divorcees accounted for 5% of the respondents. In terms of education, 35% of the participants had secondary education, while 15% had tertiary education. Primary education was reported by the 45% of the patients, as well as the 5% stated that they never had any formal education.

Looking at the occupation distribution, the majority of participants (57.5%) were self-employed. Those employed by the government constituted 25%, while 5% were students, 7.5% were housewives, and 2.5% were farmers. Additionally, 2.5% of the population consisted of other workers (Table 1).

Table 1: Socio-demographic characteristics of the study participants.

Parameters	Confirmed TB cases (105)	
	N	%
Gender		
Male	50	47.5
Female	55	52.5
Age category (in years)		
18-30	5	5
31-43	34	32.5
44-56	53	50
57-69	13	12.5
Marital status		
Single	39	37.5
Married	60	57.5
Divorced/ widow	6	5
Occupation		
Civil servants	26	25
Housewives	8	7.5
Farmers	3	2.5
Self-employed	60	57.5
Students	5	5
Others	3	2.5
Education level		
No education	5	5
Primary	47	45
Secondary	37	35
Tertiary	16	15

Hematological parameters of the study participants

the mean±SD of total white blood cell count for cases was (7.81±4.08×10^3/µl) and for controls (6.03±2.67×10^3/µl) (p=0.018). Absolute neutrophil counts (mean±SD) for cases were (4.86±3.11×10^3/µl) while for controls, the neutrophil count was (3.66±2.33×10^3/µl) (p=0.044). The mean±SD of platelet count for cases was (328.61±120.99×10^3/µl) while for controls was (272.77±69.23×10^3/µl) (p=0.009). The mean±SD of erythrocyte sedimentation rate for cases was (69.18±22.86 mm/hr) while for controls was (14.34±4.38 mm/hr) (p=0.001) (Table 2).

Red blood cell parameters

TB patients had significantly lower red blood cell counts (4.37±0.85×10^3/µl) compared to the controls

(5.10±0.82×10^3/µl) (p=0.001). There was also a significant difference in mean cell hemoglobin concentration between cases (31.50±2.19 g/dl) and controls (33.41±1.83 g/dl) (p=0.001). Similarly, the mean cell hemoglobin was significantly lower in TB patients (27.80±4.66 pg) compared to controls (29.57±2.46 pg). However, there was no significant difference in mean cell volume between cases (87.95±10.45 fl) and controls (87.97±5.50 fl) (p=0.991). Among TB patients, normocytic anemia was the most common (50%), followed by microcytic anemia (26.6%) and macrocytic anemia (23.4%).

Table 2: Levels of hematological profiles in PTB patients and controls at KTRH from February 2022 to July 2022.

Parameters	Cases mean±SD (n=105)	Controls mean±SD (n=105)	P value
RBC (10^3/ul)	4.37± 0.85	5.10± 0.82	0.001*
HGB (g/dl)	11.93± 2.01	14.60± 2.15	0.001*
HCT (%)	37.96± 6.36	44.02± 5.35	0.001*
MCV (fl)	87.95± 10.45	87.97± 5.50	0.991
MCH (pg)	27.80± 4.66	29.57± 2.46	0.028*
MCHC (g/dl)	31.50± 2.19	33.41± 1.83	0.001*
ESR (mm/hr)	69.18± 22.86	14.34± 4.38	0.001*
Platelet (10^3/µl)	328.61± 120.99	272.77± 69.23	0.009*
TWBC (10^3/µl)	7.81± 4.08	6.03± 2.67	0.018*
Neutrophil (10^3/µl)	4.86± 3.11	3.66± 2.33	0.044*
Monocytes (10^3/µl)	0.56± 0.28	0.54± 0.32	0.041*
Lymphocyte (x10^3/µl)	1.81± 0.85	2.49± 2.46	0.086

*Statistically significant hematological parameters.

Hemoglobin and hematocrit

The mean hemoglobin was lower in the TB patients (11.93±2.01 g/dl) compared to controls (14.60±2.15 g/dl). The hematocrit percentage was also lower in the TB patients (37.96%±6.36) compared to controls (44.02%±5.35). Anemia was present in 68.2% of the TB patients at the time of the diagnosis. Among the TB patients, 18.2% had moderate anemia, 47.7% had mild anemia, and 2.3% had severe anemia. In the control group, 29.5% had mild anemia, while the remaining 70.5% had normal hemoglobin levels (Figure 1).

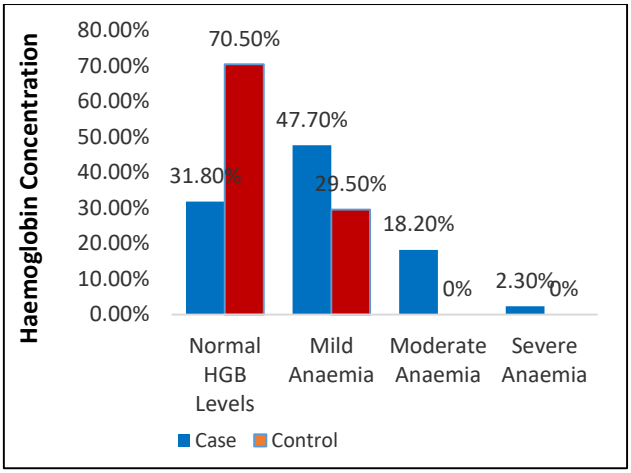

Figure 1: Severity of anemia stratified by hemoglobin concentration among study population.

Total white blood cells count

The PTB patients had a mean±SD total WBC count of (7.81±4.08×10^3/µl), while the controls had a mean±SD of (6.03±2.67×10^3/µl). Among the PTB patients, 20.5% had a total leukocyte count below the normal range (<4×10^3/µl), 63.6% had a normal total leukocyte count, and 15.9% had a count above the normal range (>11×10^3/µl). In control group, 22.7% had a leukocyte count below the normal range, 72.7% had a normal range count, and 4.5% had a count above normal range.

Absolute neutrophil count

The PTB patients had a mean ± SD A.N.C of (4.86±3.11×10^3/µl), while the controls had a mean±SD of (3.66±2.33×10^3/µl). Among the PTB patients, 13.6% had an A.N.C below the normal range (<2×10^3/µl), 68.2% had a normal A.N.C, and 18.2% had an A.N.C above the normal range (>7×10^3/µl). In the control group, 15.9% had an A.N.C below the normal range, 75% had a normal range A.N.C, and the remaining 9.1% had an A.N.C above the normal range (Figure 2).

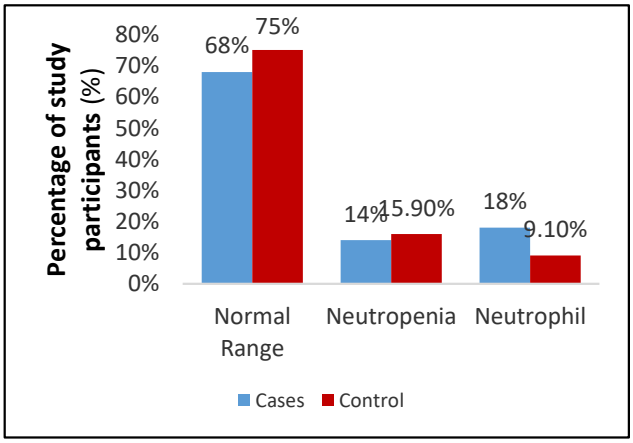

Figure 2: Absolute neutrophil count among study population.

Absolute lymphocyte count and absolute monocyte count

The mean±SD absolute lymphocyte count for pulmonary tuberculosis cases was (1.81±0.85×10^3/µl), while for the control group it was (2.49±2.46×10^3/µl). Among PTB patients, 13.6% had an ALC below (1×10^3/ul), 79.5% had a normal ALC, and 6.8% had an ALC above 3×10^3/µl. In the control group, 4.5% had an ALC below the normal range, 86.1% had a normal ALC, and 9.4% had an ALC above the normal range. The mean±SD absolute monocyte count for PTB cases was (0.56±0.28×10^3/µl), while for the control group it was (0.54±0.32×10^3/µl).

Platelet count

The mean ± SD platelet count for pulmonary tuberculosis cases was (328.61±120.99×10^3/µl), while for the control group it was (272.77±69.23×10^3/µl). Among PTB patients, 6.8% had a platelet count below (150×10^3/µl), 68.2% had a normal platelet count ranging from (150-400×10^3/µl), and 25% had a platelet count above (400×10^3/µl). In the control group, only 4.5% had a platelet count above the normal range, while the remaining 95.5% had a normal range of thrombocytes (Figure 3).

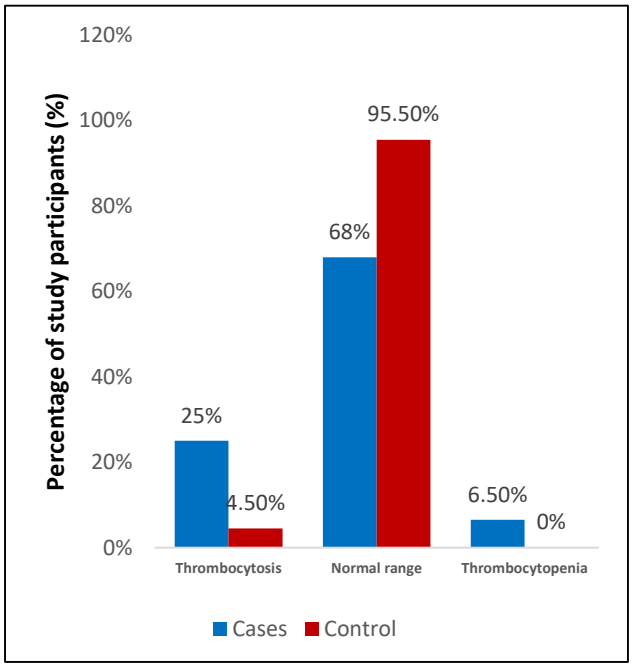

Figure 3: Platelet count among study population.

Erythrocyte sedimentation rate

The mean±SD of erythrocyte sedimentation rate for pulmonary tuberculosis cases was (69.18±22.86 mm/hr), while for the control group it was (14.34±4.38 mm/hr). ESR values were significantly higher in PTB cases compared to the control group.

Morphological changes of blood cells in peripheral blood film

Normochromic anemia was the most common hematological abnormality among pulmonary TB patients, with 55% exhibiting normocytic normochromic anemia. Other types of anemia included microcytic hypochromic (20%), normocytic hypochromic (10%), macrocytic normochromic (5%), and macrocytic hyperchromic (5%). Anemia was observed in 68.2% of the study population, with 18.2% having moderate anemia, 47.7% having mild anemia, and only 2.3% experiencing severe anemia. Toxic granulation was present in 65% of patients' white blood cells, while 25% showed the band form of neutrophils and 10% had normal WBC morphology. Most patients (95%) exhibited normal platelet morphology, while 5% had giant platelets. Thrombocytosis was indicated by higher platelet counts in PTB patients compared to the control group that is, (328.61±120.99×10^3/µl for cases and 272.77±69.23×10^3/µl for controls).

DISCUSSION

Red blood cell parameters

The reduction in RBCs could be attributed to suppressed erythropoiesis caused by inflammatory mediators and a lack of bone marrow iron. These results agree with previous studies conducted by Shafee, Abbas which reported significant reductions in RBC count and MCV, MCH, and MCHC in TB patients.[7] Rohini et al found decreased serum hemoglobin levels and RBC count in TB patients compared to healthy controls.[8]

In contrast, Yalew highlighted the insignificance of MCV as a diagnostic indicator for TB, in line with studies by Kim and Baker and Algorta that showed no significant reduction in MCV in newly diagnosed pulmonary TB patients compared to controls.[7,8,10] Thus, reduced RBC count can potentially serve as an indicator of TB infection.[12]

Hemoglobin and hematocrit

The results revealed a highly significant decrease in HGB and hematocrit values among newly diagnosed pulmonary TB patients compared to controls. These findings are in agreement with related studies conducted by Abbas which reported the significant reductions in HGB and hematocrit levels in TB patients.[7] Ufelle, Onyekwelu also found the high occurrence of the anemia among patients diagnosed with active pulmonary TB, attributing it to the anemia of chronic disease.[13] The reduction in the HGB as well as the hematocrit was associated with increased levels of interleukin-6, which can cause anemia as well as the plasma volume expansion, leading to decreased concentration in the circulating red blood cells.

Total white blood cells count

The results showed a significantly higher mean TWBC count and neutrophilia in PTB patients compared to control patients. While some previous studies reported hematological abnormalities including leukocytosis or leucopenia, neutrophilia or neutropenia, lymphocytosis or lymphocytopenia, and monocytosis or monocytopenia in PTB patients, this study observed a higher TWBC count and neutrophilia.[14] Additionally, leukocytopenia was found in 20.5% of PTB patients, normal leukocyte counts in 63.6% of patients, and leukocytosis in 15.9% of patients. These findings suggest that assessing TWBC count can provide an indication of pulmonary tuberculosis infection.[15,16]

Platelets

The study found that patients with TB had significantly higher platelet counts compared to healthy controls, which is consistent with previous studies by Mohammed.[17] However, the results contradict studies from Pakistan, which reported lower platelet counts in TB patients.[7] The increase in platelet count in TB patients may be attributed to elevated levels of interleukin-6 (IL-6), which promotes mega-karyocytopoiesis during the acute phase of infection. This finding suggests that platelet count can serve as an indicator for TB infection and aid in diagnosis and prognosis.

Limitation

Since the study was conducted at a single hospital in Kisii, Kenya, the findings may not be applicable to other populations with different demographics or access to healthcare. Additionally, the study was conducted over a period of six months and hematological profiles could vary seasonally or due to other temporal factors, which may not be adequately captured in this time frame.

CONCLUSION

The observed reductions in red blood cell count, hemoglobin, and hematocrit levels are indicative of suppressed erythropoiesis and inflammation-mediated iron restriction. Increased total white blood cell count, neutrophilia, and elevated absolute neutrophil count suggest an immune response against *Mycobacterium tuberculosis*. Additionally, elevated platelet counts and higher erythrocyte sedimentation rate further support the presence of inflammation in PTB patients.

Recommendations

Based on the study findings, healthcare professionals should consider incorporating hematological parameters into the diagnostic and monitoring protocols for pulmonary tuberculosis patients. Integrating these hematological parameters into clinical practice can contribute to more comprehensive management of pulmonary tuberculosis patients.

Additionally, large observational studies are required to establish a possible role of PTB in leukocyte alteration and its effect on the rest of biochemical values by using a larger sample size.

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