Evaluation Of Hematological Profiles In Pulmonary Tuberculosis Patients: A Case-Control Study At Metema And Gondar Referral Hospitals, North West Ethiopia

Mohammed Y Seid[1], Daniel S Maleka[2], *Araya M Kassa[1]

[1]College of Veterinary Medicine and Animal Sciences, University of Gondar, Ethiopia.

[2]Department of Biochemistry, School of Medicine, Addis Ababa University, Ethiopia.

***Correspondence:** armen.kassa@gmail.com

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ABSTRACT

Tuberculosis is one of the world's first and most common causes of death alongside HIV/AIDS, causing considerable mortality globally. Hematological alterations also accompany Tuberculosis, although the alteration related to the disease is not well determined yet and showed variation in different studies. This study aimed to evaluate hematological profiles in pulmonary tuberculosis patients in Metema hospital and Gondar referral Hospital, North West Ethiopia. A case-control study design was conducted from January to July 2018. Eighty-eight blood samples (44 from cases and 44 from control groups) were collected. The collected blood samples were tested using a Hematology analyzer (Sysmex) for hematological profiles. The mean±standard deviation of the cases' hemoglobin, hematocrit, and red blood cell count was significantly lower than the control groups ($P< 0.05$). However, platelet and total white blood cell counts; and erythrocyte sedimentation rate were significantly increased compared with control groups ($p<0.05$). Body mass index had significant positive associations with red blood cell count, hemoglobin, and hematocrit ($P < 0.05$). Pulmonary Tuberculosis patients in this study showed hematological profile abnormalities, where the red blood cell count, hematocrit, and hemoglobin were significantly reduced. However, the total white blood cell count, thrombocyte, and erythrocyte sedimentation rate of tuberculosis patients were significantly elevated than control groups. The factors associated with hematological profile alterations require attention to prevent further complications, and further studies should be conducted.

KEYWORDS: Anemia, Erythrocyte, Hemoglobin, Hematocrit Count, Leukocytes, Tuberculosis, *Mycobacterium tuberculosis*.

1. INTRODUCTION

Tuberculosis (TB) is a disease caused by bacteria called *Mycobacterium tuberculosis* [1]. TB is one of the first and most common infectious diseases leading to death alongside HIV/AIDS. It caused more than 9.6 new cases and 1.5 million deaths globally in 2014 alone [2]. TB remains a major public health problem claiming the lives of thousands of Ethiopians every year. Ethiopia is among the 22 countries with a high TB burden and 27 high Multi-Drug Resistance (MDR-Tuberculosis) TB burden countries in the world [3]. According to Abraham *et al*. (2015), an infection with TB can lead to hematological abnormalities [4]. Anemia is a cardinal feature in patients with bacterial infections, particularly infections lasting longer than a month, including PTB [5,6].

Hematological parameters, which include Red Blood Cell and White Blood Cell counts, hemoglobin and hematocrit determinations, platelet count, and RBC indices, are the backbones of any laboratory evaluation, and their abnormal values may be associated with various pathological conditions, such as tuberculosis [7]. A study in Iraq investigated the changes in some hematological parameters in patients affected with pulmonary Tuberculosis (PTB) [8].

Platelets have a role in the inflammatory response, including defense against mycobacterium [9]. Reversible mild thrombocytosis is seen in about 52% of patients with severe PTB. The elevated mean platelet count of untreated patients decreases and normalizes with successful treatment of PTB [9]. Therefore, there is a need to know those parameters of the blood which are abnormal in patients living with PTB [7]. This study was conducted to determine hematological profiles such as total leukocyte count(TLC), Platelet count, hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) using hematology analyzer.

2. METHOD(S)

2.1. STUDY AREA

The study was conducted at Metema and Gondar Hospitals in northwest Ethiopia. Metema is 896 and 158 Km away from Addis Ababa and Gondar, respectively. Gondar is 738 km away from Addis Ababa. Both hospitals (Metema and Gondar) are giving service to about 2 and 5 million people. Metema Hospital has a directly observed treatment short-course (DOTS) clinic where TB patients are treated and monitored according to the national guideline. University of Gondar Referral Hospital, in 2010, a tuberculosis isolation and treatment ward with 28 beds capacity was built to improve the hospital's tuberculosis infection control.

2.2. STUDY DESIGN AND PERIOD

A case-control study design was used to evaluate the required hematological profiles as well as assess the associated risk factors that were conducted from January to July 2018 in the study areas.

2.3. SOURCE AND STUDY POPULATION

The source population for this study was tuberculosis patients who visited Metema hospital and Gondar teaching and referral hospital. In contrast, the study population/subjects were 44 newly diagnosed TB patients and 44 healthy individuals who volunteered to participate in the study.

2.4. INCLUSION CRITERIA

Newly diagnosed TB patients, apparently healthy individuals (Not suspected of any disease), and individuals between 18-65 years old coming to both study hospitals were included in the study. Patients with hematological derangement and individuals with Diabetes mellitus, hypertension, and HIV-positive patients were excluded from the study. Written consent was taken from all participants.

2.5. SAMPLE SIZE DETERMINATION

The sample size was determined based on double population formula with the following assumption. The mean$\pm$standard deviation of lymphocytes for TB cases, 1.83$\pm$0.8, and for healthy control, 2.23$\pm$0.5 were taken from a study done in Sudan [7]. Assuming a 95% confidence interval and 80% power, and a 1:1 ratio, the minimal sample size in each group was calculated using EpiInfo software. Based on the assumption, the total sample size computed was 88, where 44 samples were from each category.

2.6. SAMPLING TECHNIQUE

Consecutive sampling methods were used for the case groups until the required sample sizes were attained, and convenient sampling techniques were used to select the control groups.

2.7. METHODS OF SAMPLE AND DATA COLLECTION

A structured questionnaire translated to the local language, Amharic, was used to collect the required data. Anthropometric measurements, including weight and height, were measured with the subjects wearing light clothing and no shoes. Body Mass Index (BMI) was calculated as kg/m^2.

2.8. BLOOD COLLECTION AND PROCESSING

After taking the consent, about 4 ml of blood was withdrawn by laboratory personnel by EDTA-coated test tubes from all the study participants. Laboratory analysis was made immediately by a hematological analyzer for CBCs and Westergren method for ESR [11,12]. Face-to-face interviews filled the questionnaire, and some anthropometric indicators were assessed and measured side by side.

2.9. DATA QUALITY CONTROL AND MANAGEMENT

Standard daily quality control protocols were performed. All instruments were operated, the quality was controlled according to the manufacturer's instructions, and normal and abnormal controls were run daily. No analysis was done if controls were out of range. Recommended quality control values for the measured parameters were used as references. Data collectors have received a half-day training about the study's objectives and how to approach participants and fill out the questionnaire. The questionnaires were pretested at Aykel and Kolladiba hospitals and then modified accordingly. The principal investigator and supervisors were supervised throughout the data collection period. Questionnaires were reviewed and checked for completeness, accuracy, and consistency by supervisors and investigators, and the blood samples were collected and processed by trained laboratory professionals.

2.10. DATA ANALYSIS AND INTERPRETATION

After checking for completeness and cleaning, processing, and analysis of the data obtained from laboratory analyses, coding was done, data was entered into Statistical Packages for Social Sciences (SPSS) software version 20, and the different variables were tested and analyzed. Simple descriptive statistics were used to present the socio-demographic and clinical characteristics of the study subjects. Continuous variables were presented as mean ± standard deviation and were compared using the independent student t-tests for groups. Other associations were tested using Pearson's correlation coefficient as well as linear regression analysis. A p-value of <0.05 at a 95% confidence level was considered statistically significant.

2.11. ETHICAL CONSIDERATION

Ethical clearance letter with reference number SOM/DRERC/BCHM073/2009 was obtained from the Departmental Research and Ethics Review Committee, Department of Biochemistry, College of Health Sciences, Addis Ababa University. A collaboration letter for data collection was also obtained from the University of Gondar and Metema Hospital. Informed consent was taken before sample collection and filling out the questionnaire. Confidentiality, anonymity, neutrality, accountability, and academic honesty were maintained.

3. RESULTS

3.1. SOCIO-DEMOGRAPHIC CHARACTERISTICS OF THE STUDY PARTICIPANTS

The study included 88 study participants, including 44 patients diagnosed with Tuberculosis with a mean ± SD of age 32.68 ± 13.44 years and 44 healthy individual volunteers participating with a mean±SD of age 32.25±10.23 years. Thirty (68.2%) were male in the case, and 27 (61.4%) were male in the control groups. Farmers (56.8% and 51.1%), married (50% and 45.5%), and income less than 500 Ethiopian Birr per month (47.7% and 47.7%) were accounted for in cases and control groups, respectively. Among the case groups, 25 (56.8%) were underweight, and 19 (43.2%) were normal weight. On the other hand, 28 (63.6%), 7 (15.9%), 6(13.6%), and 3(6.9%) of the control groups were normal weight, overweight, underweight, and obese. Twenty-three (52.3%) of the cases and 21 (46.7%) of the control had a history of alcohol drinking, and 22.7% of both groups had smoked. Nine (20.4%) of cases and 10 (22.7%) of control were alcohol and tobacco users (**Table-1**).

3.2. LEVELS OF HEMATOLOGICAL PARAMETERS IN STUDY PARTICIPANTS

The mean± SD of hemoglobin (11.93 ± 2.01 g/dL, 14.60 ± 2.15 g/dL), red blood cell (4.37 ± 0.85x 10^6/uL, 5.10 ± .82 x10^6 /uL), hematocrit (37.96± 6.36%, 44.042 ± 5.35 %) in case and control groups,respectively. Statistical significant difference was observed in hemoglobin (P = 0.001), red blood cell (P = 0.001), and hematocrit (P = 0.001). The mean± SD of mean cell volume was (87.95 ±10.45fL, 87.97± 5.50fL) in case and control groups, respectively. However, the mean reduction was not statistically significant in TB patients compared to control groups (P=0.991). The mean± SD of mean cell hemoglobin (27.80 ± 4.66pg, 29.57 ± 2.46pg), mean cell hemoglobin concentration (31.50 ± 2.19 g/dL and 33.41± 1.88 g/dL) were in case and control groups, respectively. There were statistically significant differences in MCH (P. = 0.028) and MCHC (P. = 0.001) of case and control groups, as shown in **Table-2**.

The mean±SD of total white blood cell count (7.81 ±4.08 x10^3/μL, 6.03± 2.67 x10^3/μL), absolute neutrophil counts (4.86±3.11x10^3/μL, 3.66 ± 2.33x10^3/μL), platelet count (328.61±120.99 x10^3/μL, 272.77±69.23 x10^3/μL) and erythrocyte sedimentation rate (69.18 ± 22.86 mm/hr, 14.34 ± 4.38 mm/hr) for case and control groups, respectively. There were statistically significant differences in total WBC (P=0.018), ANC (P=0.044), platelet count (P=0.009), and Erythrocyte Sedimentation Rate (P=0.001) as compared with the control. The mean ± SD of absolute lymphocytes count was (1.81±0.85 x10^3/μL, 2.49±2.46x10^3/μL), and there was no significant difference (P=0.086).

The mean±SD of hematological profiles stratified by sex are depicted in **Table-3** below. Mean Corpuscular Hemoglobin, Mean Corpuscular Hemoglobin Concentration, Total White Blood Cell, and absolute neutrophil counts were not significant in females but significant in males as compared to their male and female counterparts. Only three were insignificant in males, such as absolute lymphocyte counts, mean cell volume, and platelet counts. In contrast, in females, red blood cell counts, hemoglobin, hematocrit, erythrocyte sedimentation rate, and platelet counts were significant.

3.3. TYPE OF ANEMIA

Normocytic anemia (80-100 fL) was the most common and identified in 22 (50%) patients. While microcytic anemia (MCV < 80 fL; 26.6%) was the next common followed by macrocytic anemia (> 100 fL; 23.3%) among pulmonary tuberculosis patients. However, 42 (95.5%) control groups were normal, but only 2 individuals were shown abnormalities in Mean Corpuscular Volume.

3.4. THE SEVERITY OF ANEMIA

Overall anemia was identified in 30 (68.2%) tuberculosis patients; whereas 8 (18.2 %) moderate, 21 (47.7%) mild and 1 (2.3%) severe anemia were recorded. Contrary to this, in the control group, only mild anemia 13(29.5%) was observed (**Figure-1)**.

3.5. TOTAL LEUKOCYTE COUNT

Out the PTB patients, 9 (20.5%) had total leukocyte count below 4.0 $x10^3$/uL (leukocytopenia), 28 (63.6%) had normal total leukocyte count and 7 (15.9%) of tuberculosis patients had above 11.0 $x10^3$/uL (leukocytosis). However, in the control groups, 10(22.7%) revealed below normal (leukocytopenia), 32(72.7%) normal, and 2 (4.5%) above the range (leukocytosis).

3.6. ABSOLUTE NEUTROPHIL COUNT (ANC)

Of PTB patients, 6 (13.6 %) had ANC below (neutropenia), 30 (68.2%) had normal ANC and 8 (18.2%) had ANC above normal range (neutrophilia); where as in the control groups 7(15.9%) were below normal (neutropenia), 32(75%) within the normal range while the remaining were 4(9.1%) above the normal range (neutrophilia) (**Figure-2)**.

3.7. ABSOLUTE LYMPHOCYTE COUNTS

Six 6(13.6%) of the pulmonary tuberculosis patients had absolute lymphocyte count below (lymphopenia), and 3(6.8%) had absolute lymphocyte count above (lymphocytosis) in the normal range, while the rest showed normal readings. From the control groups, 2(4.5%) were below normal (lymphopenia) and 4(9.1%) were above normal lymphocyte range (lymphocytosis), while the rest were within the normal ranges.

3.8. PLATELET COUNTS

In this study, thrombocytopenia was recorded in 3 (6.8%) PTB cases, while thrombocytosis was observed in both cases, where it was 11 (25.0%) in PTB patients and 2 (4.5%) in the control groups (**Figure-3)**.

3.9. FACTORS ASSOCIATED WITH HEMATOLOGICAL PROFILES

Pearson correlation, analyses showed that,status of study participants at the time of diagnosis were showing positive correlation between being case and total White Blood Cell count ($r=0.25$, $p< 0.05$), platelet count ($r=0.27$, $p<0.05$), and Erythrocyte Sedimentation Rate ($r=0.86$, $p< 0.05$) but being a case was negatively correlated with Red Blood Cell count ($r= -0.40$, $p<0.05$), haemoglobin ($r= -0.54$, $p <0.05$) and haematocrit ($r= -0.54$, $p <0.05$). Linear regression analysis also showed that 6.4%, 16.3%, 29.5%, 27.3%, 7.6%, and 73.9% of the variation in total White Blood Cell, Red Blood Cell, hemoglobin, hematocrit, platelets, and erythrocyte, respectively were explained by being a case or control.

In this study, age at the time of diagnosis was negatively correlated with total White Blood Cell ($r= -0.23$, $p < 0.05$), Red Blood Cell ($r = -0.141$, $p>0.05$); hemoglobin ($r = -0.079$, $p > 0.05$); hematocrit ($r = -0.103$, $p > 0.05$) and platelet ($r = -0.023$, $p > 0.05$). Erythrocyte ($r= 0.156$, $p > 0.05$) was positively correlated with age in the PTB patients. Linear regression analysis also showed 5.4%, 2.3%, 0.6%, 1.1%, 0.1%, and 2.4% variations in total White Blood Cell, Red Blood Cell, hemoglobin, hematocrit, platelet, and Erythrocyte Sedimentation Red, respectively were explained by age.

The Body Mass Index was negatively correlated with Total White Blood Cell count, Platelet count, and Erythrocyte Sedimentation Rate. However, Red Blood Cell counts, hemoglobin, and hematocrit were positively correlated. Linear regression analysis also showed that 0.1 %, 1.1 %, 0.1 %, and 5.7% of the variations of total White Blood Cell, Red Blood Cell, hematocrit, and platelet, respectively, were explained by body mass index.

4. DISCUSSION

Tuberculosis is one of the most important communicable diseases in the world. Various hematological profile alterations have been described in association with Tuberculosis. Significantly larger proportions of the patients were found to have decreased levels of hematological parameters such as hemoglobin, hematocrit, Red Blood Cell counts, as well as Red Blood Cellindices such as Mean Corpuscular Hemoglobin, Mean Corpuscular Hemoglobin Concentration, and anthropometric indicators like body mass index were also decreased in patients compared with control groups. Platelet counts, erythrocytes, and total White Blood Cell counts were also higher in tuberculosis patients than in control groups. Furthermore, the present study indicated that hemoglobin, hematocrit, red blood cell count, and red blood cell indices like mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration showed statistically significant differences among Infected patients ($P\leq0.05$)compared to the control groups. On the contrary, pulmonary tuberculosis patients had statistically significantly higher levels of circulating platelets, erythrocyte sedimentation rate, and white blood cell counts ($P < 0.05$) compared to the control group. These results are in agreement with the results of other related studies, which are conducted in different parts of the world, including Ethiopia, where statistically significant mean reduction of hemoglobin, hematocrit, and Red Blood Cell indices of tuberculosis patients was reported [7,10,13,14].

In this study, the mean±SD of red blood cells in tuberculosis patients was (4.37 ± .85 x10^6 /uL) and the control group was (5.10 ± .82 x10^6 /uL) which also showed a significant decrease when compared with controls (P< 0.05). These findings were also supported by the reports made by other related studies [10,15]. The possible explanation for this Red Blood Cell reduction might be due to the suppression of erythropoiesis by inflammatory mediators' that display an absence of bone marrow iron [16].

In the current study, 26.8% of patients had decreased Mean Corpuscular Hemoglobin. In comparison, 23.3% of patients had increased value, although the difference was not statistically significant, and this finding coincides with other studies [7,10, 17,18]. The present study showed a statistically significant (p <0.05) mean reduction in the value of mean cell hemoglobin and mean cell hemoglobin concentration in newly diagnosed PTB patients in comparison with healthy controls, and this is in agreement with similar studies [7,18].

Anemia occurred in 30 (68.7%) of the study populations. This finding is in line with reports by Yaranal et al., who reported that 74(68.9%) patients had anemia. However, the report by Yaranal et al. reveals that 49 (66.2%) patients have normocytic anemia [19]. In the current study, normocytic anemia was the most common type, accounting for 22 (50%) patients. The severity of anemia was determined as the result of hemoglobin level by which (18.2%) of total patients had moderate anemia and (47.7%) had mild anemia, and only (2.3%) of patients had severe anemia. This finding agrees with a similar study done in 2009 [20].

There was a highly significant (p < 0.05) decrease in the hemoglobin and hematocrit values in the newly diagnosed PTB patients in comparison with healthy controls, which is in agreement with studies done by Eyshi *et al.*, who state that the occurrence of anemia among patients that were diagnosed as active PTB is very high. It contributes to anemia of chronic disease [6]. This reduction might be associated with an increased level of interleukin-6 (IL-6).

In this study, 20.5% of PTB patients showed decreased leukocyte count (leukocytopenia), 63.6% were normal, and 15.9% increased leukocyte count (leukocytosis). These findings agree with a similar study done in Sudan [7]. However, it disagrees with Mohammed *et al.*, 2016, where there is no statistically significant difference in the occurrence of leukopenia or leukocytosis between PTB positive and negative patients (p=0.005). However, among the 15 leukopenic patients, 12(80.0%) were PTB patients, as diagnosed by GeneXpert, which is remarkable [14]. Absolute neutrophil count was significantly increased in PTB patients compared with control groups; this result agrees with a similar study [7]. This study indicated a significant increase in total leukocyte count among PTB patients. That increase might be due to an immune reaction to foreign antigen Mycobacterium tuberculosis that increased cytokine levels [4].

In this study, the values of platelet count in PTB patients were significantly increased (p = 0.009) compared with their counterparts. These results might be related to Abaker *et al.*'s (2015) idea that reactive thrombocytosis is found in several clinical situations, including infectious diseases such as PTB [7], which also agrees with Al-Omar *et al.* (2009), where the increase in platelet count was noticed in Saudi PTB patients as compared with the normal Saudi persons [20]. However, the current results have been in contrast with similar research done in Pakistan and Nigeria, where they reported lower platelet counts in PTB patients [21,22].

In this work, it has been found that the values of erythrocyte sedimentation rate for PTB patients increased significantly (p< 0.001) compared with healthy controls. This finding was supported by different reports and studies, which specify high erythrocyte sedimentation rate levels in newly diagnosed and normal levels at the end of treatment of PTB patients who state that erythrocyte sedimentation rate is elevated in PTB [20]. Awodu *et al.* stated that the erythrocyte sedimentation rate is significantly higher in PTB patients than in controls. However, after the fourth week of therapy, there is a significant reduction in the erythrocyte sedimentation rate of PTB patients [22]. Olaniyi *et al.* indicate statistically significant hematologic abnormalities like high erythrocyte sedimentation rate in PTB patients in Ibadan, Nigeria [23].

In the present study, being a case has a significant association with most hematological alterations among study participants. It negatively affected most hematological profile levels except for white blood cells, platelets, and erythrocyte sedimentation rate. The inverse association of PTB disease to hematological profiles like Red Blood Cell, hemoglobin, hematocrit, and Red Blood Cell indices were supported by different studies carried out by various researchers, which demonstrated a statistically significant mean reduction in PTB patients compared to healthy control groups [11,24].

5. CONCLUSION

The present case-control study indicated hematological profile abnormalities in PTB patients. In the majority of PTB patients, mild and normocytic anemia was found. Total White Blood Cell counts and absolute neutrophil counts were significantly increased in PTB patients compared to control groups. Erythrocyte sedimentation rate and platelet counts were also significantly increased in PTB patients. Assessing selected hematological profiles of PTB patients could be used as a diagnostic tool, case management, and monitoring.

5.1. LIMITATION OF THE STUDY

Smaller sample utilization and lack of checking for tuberculosis-HIV coinfection in the current study could be considered limitations.

CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

All authors equally contributed to the study.

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Table-1: Socio-demographic characteristics of the study participants at Metema and Gondar Referral Hospitals, Northwest Ethiopia, 2018(n=88).

No.	Variables	Case (44)	Control (44)
		Frequency (%)	Frequency (%)
1	**Sex**		
	Male	30 (68.2%)	27 (61.4%)
	Female	14 (31.8%)	17 (38.6%)
2	**Age (Yrs)**		
	18-24	11(25%)	10 (22.7%)
	25-34	19 (43.2%)	20 (45.5%)
	35-44	7 (15.9%)	9 (20.5%)
	≥ 45	7 (15.9%)	5 (11.4%)
3	**Marital status**		
	Married	22 (50%)	20 (45.5%)
	Divorced	3 (6.8%)	3 (6.8%)
	Single	16 (36.4%)	17 (38.6%)
	Widowed	3 (6.8%)	4 (9.1%)
4	**Residence**		
	Rural	22 (50%)	22 (50%)
	Urban	22 (50%)	22 (50%)
5	**Occupation**		
	Daily laborer	5 (14.4%)	3 (8.9%)
	Students	5 (14.4%)	6 (13.3%)
	Civil servant	2 (6.8%)	4 (8.9%)
	Merchant	3 (4.5%)	3 (6.7%)
	Farmer	25 (56.8%)	23 (51.1%)
	Others	4 (9.1%)	5 (11.1%)
6	**Educational level**		
	Illiterate	14 (31.8%)	17 (38.6%)
	Elementary	21 (47.7%)	11(25%)
	High school	3 (6.8%)	11 (25%)
	College	6 (13.6%)	5 (11.4%)
7	**Income**		
	< 500	21 (47.7%)	21(47.7%)
	500-1000	9 (20.5%)	8 (18.2%)
	1001-2000	8 (18.2%)	12 (27.3%)
	> 2000	6 (13.6%)	3 (6.8%)
8	**Family size**		
	<3	18 (40.9%)	20 (45.5%)
	3 – 5	14 (31.8%)	16 (36.4%)
	> 6	12 (27.3%)	8 (18.2%)
9	**BMI**		
	Underweight	25 (56.8%)	6 (13.6%)
	Normal	19 (43.2%)	28 (63.6%)
	Overweight	0	7 (15.9%)
	Obese	0	3 (6.9%)
10	**Smoking status**		
	Yes	10 (22.7%)	10 (22.7%)
	No	34 (77.3%)	34 (77.8%)
11	**Alcohol use**		
	Yes	23 (52.3%)	21 (46.5%)
	No	21 (47.7%)	23 (53.3%)
12	**Alcohol and smoke users**	9 (20.4%)	10 (22.7%)

Table-2: Levels of hematological profiles in PTB patients and apparently healthy controls at Metema and Gondar Referral Hospitals, Ethiopia, 2018 (n=88).

Variables	Cases (n=44)	Controls (n=44)	P-value
Red blood cell(10^6/uL)	4.37± .85	5.10 ± .82	**0.001***
Hemoglobin (g/dL)	11.93 ± 2.01	14.60 ± 2.15	**0.001***
Hematocrit (%)	37.96± 6.36	44.02 ±5.35	**0.001***
Mean corpuscular volume (fL)	87.95 ±10.45	87.97± 5.50	0.991
Mean corpuscular hemoglobin (pg)	27.80 ± 4.66	29.57 ± 2.46	**0.028***
Mean corpuscular hemoglobin concentration (g/dL)	31.50± 2.19	33.41 ± 1.83	**0.001***
Erythrocyte (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***
Total white blood cell count(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***
Lymphocyte(x10^3/µl)	1.81±0.85	2.49±2.46	0.086

*Values are expressed as mean ± standard deviation; *The mean difference is significant at P ≤ 0.05

Table 3: Levels of hematological parameters among Male and female study participants at Metema and Gondar Referral Hospitals, Ethiopia, 2018 (n=88).

Variable	Male (n=57)			Female (n=31)		
	Case (30)	Control (27)	P value	Case (14)	Control (17)	P value
RBC$^+$(x10^6/uL)	4.55 (0 .70)	5.35(0.83)	**0.001***	3.98(1.03)	4.70(0.62)	**0.023***
HGB$^+$ (g/dL)	12.28 (1.90)	15.37(2.07)	**0.001***	11.17(2.11)	13.38(1.70)	**0.003***
HCT$^+$(%)	39.36 (5.57)	46.04(5.27)	**0.001***	34.97(7.10)	40.80(3.74)	**0.007***
MCV$^+$ (fL)	87.19 (9.77)	87.67(4.16)	0.625	89.59(12.0)	88.45(7.26)	0.748
MCH$^+$ (Pg)	27.28 (4.38)	29.53(2.06)	**0.018***	28.90(5.19)	29.64(3.05)	0.625
MCHC$^+$ (g/dL)	31.20 (2.02)	33.55(1.68)	**0.001***	32.15(2.48)	33.17(2.09)	0.222
ESR$^+$ (mm/hr)	68.63(23.65)	15.48(4.81)	**0.001***	70.36(21.9)	12.53(2.89)	**0.001***
Platelet(10^3/µL)	311.2(108.5)	264.85(66.4)	0.060	365.93(141)	285.35(73.76)	**0.050***
TWBC$^+$(10^3/µL)	7.46(2.83)	5.71(2.25)	**0.013***	8.57(3.01)	6.55(3.23)	0.243
Neutrophil(10^3/µl)	4.61(2.16)	3.49(1.76)	**0.038***	5.40(4.60)	3.94(3.06)	0.301
Lymphocyte(10^3/µl)	1.76(0.75)	2.79(3.09)	0.082	1.92(1.06)	2.02(0.67)	0.750

Values are expressed as mean ± standard deviation; *The mean difference is significant at P ≤ 0.05

NB: $^+$Please refer to Table-2 for the description of the abbreviations.

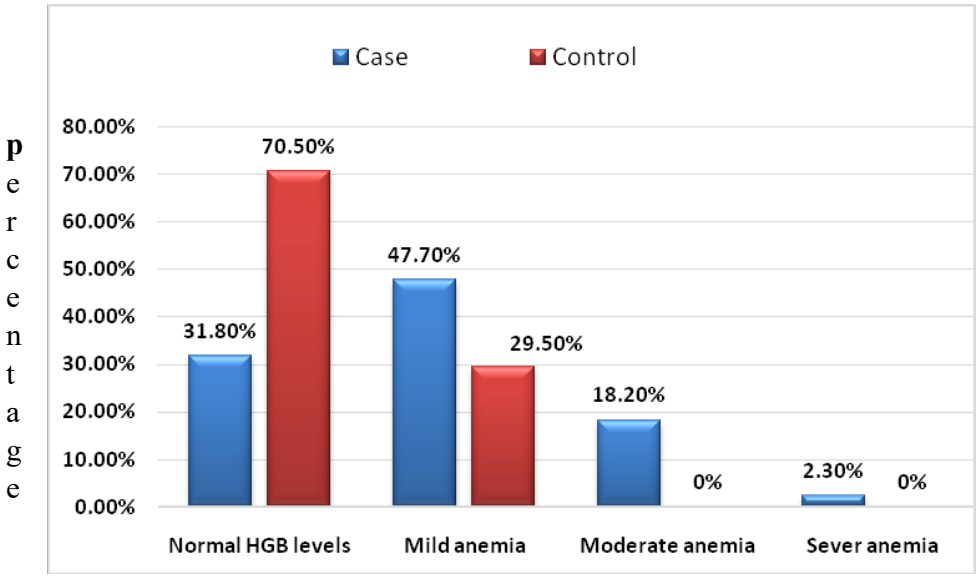

Figure-1: Severity of anemia stratified by hemoglobin concentration among study population at Metema and Gondar Referral Hospitals, Ethiopia, 2018.

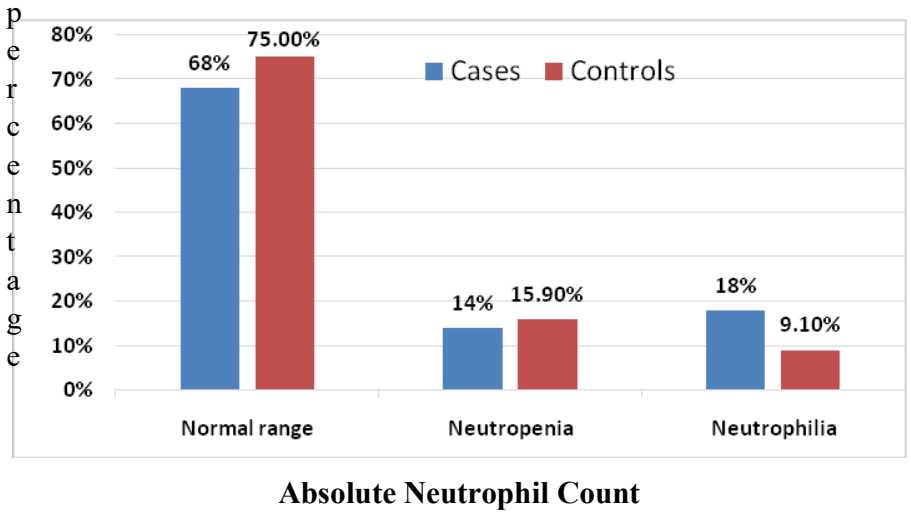

Figure-2: Absolute neutrophil count among study population at Metema and Gondar Referral Hospitals, Ethiopia, 2018.

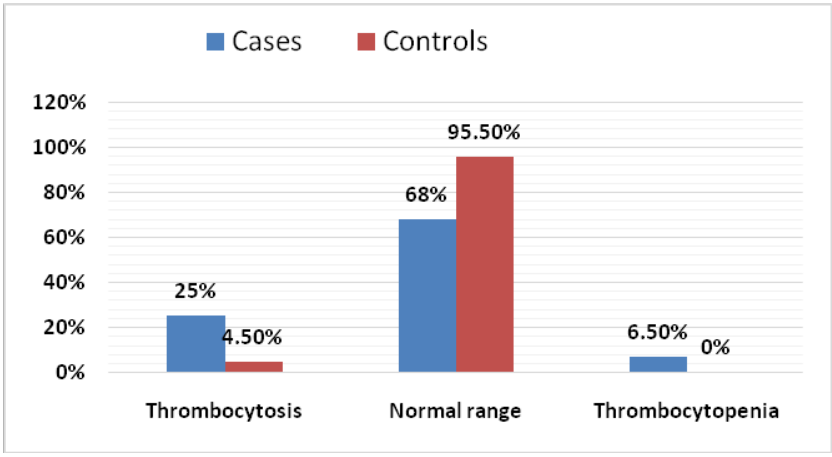

Figure-3: Platelet count among study population at Metema and Gondar Referral Hospitals, Ethiopia, 2018.