ASSESSMENT OF HEMATOLOGICAL PARAMETER ABNORMALITIES AND ASSOCIATED FACTORS AMONG PREECLAMPTIC PREGNANT WOMEN ATTENDING CHIRO, AND GELEMSO GENERAL HOSPITALS: A COMPARATIVE CROSS-SECTIONAL STUDY.

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A THESIS SUBMITTED TO SCHOOL OF MEDICAL LABORATORY SCIENCE, FACULTY OF HEALH SCIENCES, INSTITUTE OF HEALTH, JIMMA UNIVERSITY IN PARTIAL FULFILLMENTS OF THE REQUIREMENTS FOR MASTERS OF SCIENCES DEGREE IN CLINICAL LABORATORY SCIENCE, SPECIALTY IN HEMATOLOGY AND IMMUNOHEMATOLOGY

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JIMMA, ETHIOPIA

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Abstract

Background: *Pre-eclampsia is one of the most common causes of maternal and fetal complications, as well as hematological abnormalities, and is a multisystem dependent disorder worldwide. As a result, determining hematological parameters and related factors among pre-eclamptic pregnant women is crucial for the management of the condition.*

Objective *To assess hematological parameters, abnormalities and associated factors among pre-eclamptic pregnant women attending Chiro and Gelemso General Hospitals from November 15, to Feb 15, 2022, Eastern Ethiopia.*

Methods: - Institution-based Comparative Cross-sectional study design *was conducted among 97 preeclamptic and 97 normotensive controls, by using consecutive sampling technique. Socio-demographic and Clinical data were collected by interviewing & from logbooks, respectively. Four (**4ml**) of blood samples were collected with K2-EDTA tube and gently mixed and analyzed for CBC by using hematology auto analyzer, **Sysmex-XN-550**. Then, entered into Epi-Data software version 3.1, and exported to SPSS software version 25.0 for analysis ($p<0.05$). An independent sample t-test and Mann-Whitney U test was used to compare the mean of hematological parameters of the study groups. Receiver operator Characteristic analysis was done to determine AUC, sensitivity, and specificity among hematological parameters for preeclampsia diagnosis.*

The result *of the study revealed that, a total of 97 patient's age ranging from 17 to 37 years with a mean age of 27.09 ± 4.98 years for preeclampsia and 26.99 ± 4.92 years for the control group were included. In preeclamptic women, the mean platelet count was 147.1 ± 86.4 (x 10^9/L), when compared to 248.22 ±62(x 10^9/L) in controls, ($p < 0.05$). The prevalence of Anemia among preeclamptic women was significantly higher 39(40.21%), while the magnitude of thrombocytopenia was 68(70%).*

Conclusion: - *The present study, thrombocytopenia had the highest prevalence 68/97 (70%) among preeclampsia, followed by anemia 39/97(40.21%). The majority of hematological parameters in the study between preeclamptic and normotensive pregnant women revealed statistically significant variations.*

Keyword: *Hematological parameters, Pre-eclamptic, Normotensive pregnant women, Chiro, Gelemso, Hospitals.*

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LIST OF ABBREVIATIONS

ANC	=	Absolute Neutrophil Count / Antenatal care
ANOVA	=	Analysis of variances
BMI	=	Body Mass Index
CBC	=	Complete blood count
DBP	=	Diastolic Blood Pressure
EDHS	=	Ethiopian Demographic and Health Survey
EDTA	=	Ethylene Diamine Tetra Acetic acid
HELLP	=	Hemolysis Elevated Liver enzyme and Low Platelet
IQR	=	Interquartile Range
LBW	=	Low Birth Weight
MAP	=	Mean Arterial Pressure
MCV	=	Mean Cell Volume
MCH	=	Mean Corpuscular Hemoglobin
MCHC	=	Mean Corpuscular Hemoglobin concentration
NLR	=	Neutrophil-Lymphocyte Ratio
PDW	=	Platelet Distribution Width
PE	=	Preeclampsia
PLCR	=	Platelet Large-Cell Ratio
RBC	=	Red Blood Cell
RDW	=	Red Cell Distribution Width
ROC	=	Receiver Operating Characteristic
SBP	=	Systolic Blood Pressure
WBC	=	White Blood Cell
WHO	=	World Health Organization

1. INTRODUCTION

1.1. Background

Preeclampsia (PE) is a pregnancy disorder which is defined as a systemic syndrome characterized by a new onset of hypertension (blood pressure – systolic > 140 mm Hg, diastolic > 90 mm Hg on two occasions at least 4h apart, or in severe cases systolic blood pressure > 160 mm Hg and diastolic blood pressure > 110mm Hg and proteinuria after 20 weeks of gestational age in pregnant women (1). The pathophysiology of pre-eclampsia is assumed to be complicated, as it involves interactions between various genetic, immunologic, and environmental variables (2).

Pregnancy complications caused around 289,000 deaths of women worldwide and 99% of them were from developing countries(3). As estimated by WHO, the occurrence of preeclampsia is seven times higher in developing countries compared to developed countries(4). In developing countries, women are at a 14 times higher risk of dying from obstetric complications compared to developed countries(5).

Pregnancy anemia is the most common nutritional problem, and it has substantial short- and long-term effects on both the mother and the fetus(6). Thrombocytopenia is a common hematological disorder during pregnancy next to anemia. Complications of thrombocytopenia in pregnancy include severe bleeding during or after childbirth, leaking at the site of a cesarean section, stillbirth, and neonatal thrombocytopenia(7).

The pathophysiology of preeclampsia is still not fully understood, however hemostatic alterations such as endothelial cell injury, platelet activation, and enhanced intravascular thrombin production have been known to be the primary events(8). The proposed pathogenesis of pregnancy-related preeclampsia involves abnormal placentation caused by insufficient fetal trophoblast invasion of uterine tissue to remodel the uterine spiral arteries, followed by the onset of placental ischemia or insufficient placental perfusion, followed by progressive ischemia or hypoxia (9, 10).

In a normal pregnancy, a slight increase in platelet aggregation is seen, which is compensated by an increase in platelet production(11). Endothelial damage is a feature of preeclampsia, and the predicted effects include increased platelet destruction and uncontrolled intravascular platelet activation (8).

Anemia during pregnancy is a significant public health issue, particularly in developing nations and it increases maternal mortality and, as a risk factor for preeclampsia, it increases maternal and perinatal morbidity(12). Red cell distribution width is a measure of anisocytosis and exhibits fluctuation in red blood cell volume; it is particularly useful for identifying iron deficiency anemia and also increases in cases of nutritional deficiencies of vitamin B12 and folate (13).

When compared to a normal pregnancy, the activation of platelets, leukocytes, and systemic endothelial cells is heightened in preeclampsia, and their interaction is thought to cause vascular damage(9), and leukocyte activation is known to play a significant role in the development of preeclampsia(14). Recent research suggests that measuring hematological markers such as blood cell counts and subtypes may provide prognostic and diagnostic clues for diseases affecting both mothers and babies (15).

Since preeclampsia's etiology remains unknown, investigation and identification of the most important hematological parameters abnormalities, and associated factors are vital for policymaking and clinical purposes including prioritization of interventions, resource allocation, and identification of high-risk pregnant women for more intensive observation and care, and development or improvement of risk management strategies through a practically evidenced laboratory test.

1.2. Statement of the problem

Anemia is the most typical hematologic complication during pregnancy. It is a widespread public health problem that significantly affects expectant mothers, and its prevalence is 16.6%(16). The most prevalent hematologic condition in pregnancy, aside from anemia, is thrombocytopenia, which affects 6% to 10% of all pregnant women(17).

Serious complications of preeclampsia, include severe preeclampsia, hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome, and eclampsia occurs in about 5 to 6 deliveries per 1000(18). Preeclampsia may present with various hematological features, variating from normal laboratory tests to severe thrombocytopenia (due to platelet activation and consumption), and/or anemia (19). The risk of developing anemia in preeclamptic pregnant women was significantly increased with the severity of the disease condition (20).

The complication of preeclampsia affects not only the mothers but also the fetus and the newborns; which includes premature delivery, intrauterine growth restriction (IUGR), abruptio placentae, and intrauterine death (21). Maternal complication associated with hematological abnormalities includes; Hemolysis, elevated liver enzymes, and low platelet (HELLP syndrome), pulmonary edema, acute liver /renal failure, disseminated intravascular coagulopathy(DIC), sepsis and liver hemorrhage (22).

Platelets release more than 300 active chemicals from their intracellular granules when they are activated. The alpha and dense granule components that the activated platelets secrete and release help to promote platelet aggregation(23). Additionally, the damaged vascular endothelium releases tissue factor, which starts the coagulation process (24).

Pregnant women with thrombocytopenia have a higher risk of bleeding excessively during or after childbirth, particularly if they need to have a cesarean section or other surgical intervention during pregnancy, labor, or in the puerperium (25). Platelets are key players in hemostasis and thrombus formation. Defects affecting platelets during pregnancy can lead to heterogeneous complications, such as thrombosis, first- trimester miscarriage, and postpartum hemorrhage that complicates preeclamptic conditions (26).

Even though, the exact pathophysiology of preeclampsia is not fully understood, the function of different platelets indices; like Plateletcrit (PCT), mean platelet volume (MPV), and platelet distribution width (PDW) utilized to predict preeclampsia and are considered as markers of platelet activation (27). Preeclamptic pregnancy is related to an enhanced maternal inflammatory condition, which is reflected in fetal circulation. This enhanced inflammatory state appears to be related to endothelial dysfunction and increased cytokine synthesis, rather than with neutrophil activation (28).

Preeclamptic pregnant women had increased number of leucocytes, especially neutrophil counts, since it is the common inflammatory marker of white blood cell population (29). Pregnant women with severe preeclampsia most likely had leukocytosis however, they had lower lymphocyte and monocyte among WBC population(30).

There were lots of poor pregnancy outcome associated with preeclampsia including both maternal and neonatal outcomes. However, there is a disease burden due to preeclampsia and limited study regarding hematological parameters among preeclamptic women in study area as well as in the country. Taking this into consideration, the study aims to assess hematological parameters abnormalities and associated factors among preeclampsia in comparison with normotensive pregnant women attending at Chiro, and Gelemso General Hospitals, west Hararge, Oromia Regional States, Ethiopia.

1.3. Significance of the study

The aim of this study was conducted to show the magnitude of hematological parameters abnormalities and the mean difference of hematological parameters among preeclampsia and normotensive pregnant women.

It aids clinicians and health caregivers in detecting and effectively managing disease complications earlier.

The finding of this study could be used as a baseline data for the health institution.

It could also be used as a baseline data for the researchers to elaborate further study concepts linked with preeclampsia and hematological abnormality at local, regional and national levels.

2. LITRATURE REVIEW

Preeclampsia is associated with the alteration of hematological profiles, of which thrombocytopenia is the most common which may be accompanied by a clinically evident consumptive coagulopathy(31). White blood cells are positively associated with inflammation and the abnormality detected in RBC indices; Red ell distribution width (RDW), hemoglobin (Hb), hematocrit (Hct), mean corpuscular hemoglobin (MCH), are also used to detect and investigating anemia, which is the common complication in preeclamptic as well as normal pregnancy(32, 33).

2.1. Hematological abnormalities among pre-eclamptic and normotensive pregnancy

Anemia is the most typical hematologic complication during pregnancy. The term "physiologic anemia of pregnancy" refers to a number of normal physiological processes that take place throughout pregnancy. The decrease in hemoglobin concentration is explained by an increase in plasma volume (40–50%) compared to red cell mass (20–30%).

The large retrospective study conducted in China 2018, shows the association between hemoglobin level and preeclampsia. According to the study Hemoglobin levels greater than 150 g/L or 15.0 g/dl in first trimester were indicating increased risk in pregnancy complication with pre-eclampsia compared with controls. (34).

Study conducted in Makassar City, Indonesia, also showed that women with severe preeclampsia most likely had leukocytosis than normotensive pregnant women. However, they had lower lymphocyte and monocyte among WBC population(30). According to the study conducted in Irbil, Maternal Teaching Hospital Iraq 2020, the mean platelets value was significantly lower in patients with preeclampsia (73.58 ± 26.05) compared to the controls (262.05 ± 81.01)(35).

Another comparative cross-sectional study conducted in Lahore, Pakistan, in 2018, the mean platelets count in preeclamptic and normotensive pregnant women was 219.43±100.58 and 254.43±70.35 respectively(36).

According to the cross-sectional study conducted from January to July 2017 at a tertiary care hospital in Delhi, India 2017, the values of RDW and MPV were higher in pregnant women with

pre- eclampsia. Whereas the value of platelet count was decreased, and this study demonstrated that RDW and MPV can be used as a marker of subclinical inflammation(37).

Another retrospective case-control study conducted with 186 patients in Ankara, Turkey 2019, the white blood cell and neutrophil counts were higher in Early -Onset Pre-eclampsia (EOPE) when compared with the Late-Onset pre-eclampsia of the study participants. The study also reveals that optimum cut-off value for WBC and Neutrophil were $9.55\times10^3/\mu L$ (sensitivity 71.4% and specificity 70.7%) and $6.45\times10^3/\mu L$ (sensitivity 66.7% and specificity 74.8%), respectively (38).

According to the Hospital based Cross-sectional study conducted in Sanliurfa, Turkey, in 2016, the prevalence of preeclamptic patients in the study were anemic (blood Hb <11 g/dL) which is 25%. Their average values of Hematocrit(Hct) and Hemoglobin (Hb) were 35.33±4.05%, and 11.93±1.49 g/dL respectively (39). And a retrospective case-control study conducted with 186 patients in Ankara, Turkey, showed that an increased level of red cell distribution width (RDW) were revealed to be linked with inflammation in the general population with pre-eclampsia (38).

As the case control study conducted in Aydin Turkey, in preeclampsia and severe pre-eclampsia the median red cell distribution width (RDW) was elevated 15% (13.8-16.57). On the other hand, the mean MCV value was decreased (80.42±7.86) fL and the mean MCHC value was 33.66±1.71 (g/ dL) in pre-eclamptic mothers, i.e., RDW were elevated as the severity of pre-eclampsia increases, whereas MCV decreases as the disease severity increases (40).

According to the retrospective secondary analysis of an observational study conducted at Dublin, Ireland 2017, of the 15,299 deliveries during the study period, 334 (2.2%) pregnancies had complicated by preeclampsia. And from those study participants ($n = 294$) were demarcated as late onset preeclampsia developing after 34 weeks' gestational age and the remaining 40 women were categorized as early onset pre-eclampsia. This study had shown that MPV has increased when the patients were clinical diagnosis for early onset preeclampsia (9.0fl), but not at first trimester (8.1fl) (41).

According to the study conducted in Nigeria the mean total white blood cell (WBC) count was $(7.35 \pm 5.54) \times10^9/L$ and $(5.09 \pm 2.07) \times10^9/L$ among preeclampsia and normotensive pregnant women respectively (29). A cross-sectional study conducted in Gondar University, Ethiopia

2018, shown that in preeclamptic women there was an elevated value of mean (±SD) of white blood cell (WBC), and absolute neutrophil count (42).

According to the comparative cross-sectional study conducted at Ayder comprehensive specialized and Mekelle general hospitals, Mekelle, Tigray, Ethiopia 2019, demonstrated that there were a close association between decreased platelet count with increased severity of preeclampsia (mild PE and severe PE), but no association between platelet indices (MPV, PDW and P-LCR) (9).

2.2. Factors associated with hematological abnormalities among pre-eclamptic and normotensive pregnancy

According to the study conducted in Rift valley University, Alkan and Bahir Dar health science college Bahir dar, Ethiopia in the year 2014, eating habits of vegetables or fruit had lower the risk of developing anemia due to preeclampsia than women who were not (43).

According to the case control study conducted in India, in 2018, the advanced maternal age, severe anemia, twin pregnancy and rural residence and low educational level has been the independent risk factors for hematological abnormalities due to pre-eclampsia which contribute the complication of maternal outcomes, low birth weight (LBW) and still births in anemic women and intra uterine growth restriction (IUGR) in severe pre-eclamptic women (44).

A descriptive-analytic and case-control study which was performed on 100 hypertensive nulliparous women in Mashhad, Iran 2010 most of the nulliparous mothers (49%) had severe preeclampsia (blood pressure >160/110 and 24-h urine protein >300mg), 17% of the patients had mild preeclampsia (blood pressure <160/110mmHg and 24-h urine protein >300mg). This study also reveals that mean gestational age(35.37±2.25)week, mean low birth weight (2483±653.22gm) and intra uterine growth restriction are the risk factors associated with hematological abnormalities that caused by severe pre-eclampsia (45).

According to the population based study conducted in Canada in 2021, younger mothers (aged < 25 years) were at high risk for severe preeclampsia at term and for eclampsia at all gestational ages, whereas old mothers (aged ≥ 35 years) had elevated risks for severe preeclampsia, hemolysis, elevated liver enzymes, and low platelet count syndrome (46).

3. OBJECTIVES

3.1. General Objective

To assess hematological parameter abnormalities and associated factors among preeclamptic and normotensive pregnant women attending Chiro and Gelemso General Hospitals, from November 15, to Feb 15, 2022

3.2. Specific Objectives

- To assess hematological parameters among pre-eclamptic and normotensive pregnant women.
- To assess the best potential predictor of pre-eclampsia among hematological parameters.
- To identify factors associated with hematological abnormalities among pre-eclamptic pregnant women.

4. MATERIALS AND METHODS

4.1. Study area and period

The study was conducted at Chiro and Gelemso General Hospitals, West Hararge, Ethiopia, from November 15, to Feb 15, 2022. Chiro town the capital of west Hararge zone is located 326 km to the East direction, away from the capital city of Ethiopia, Addis Ababa. Gelemso general Hospital is also located 70km away from Chiro town to the southern direction. According to West Hararge zonal health department report of 2021, there are a total of 2,867,000 populations found in the zone. From the total population, about 1,446,835 and 1,420,165 were male and female, respectively. Chiro general hospital serves 1,807,922 populations, of whom 13,833 were expected to be women of childbearing age. Gelemso general hospital also serves 1,059,078 people, of whom 12,426 were estimated to be women of childbearing age.

4.2. Study design

Institution based Comparative Cross- Sectional study was conducted.

4.3. Population

4.3.1. Source population

The source population was all preeclamptic pregnant women attending Chiro and Gelemso General Hospitals, and gestational age matched healthy pregnant controls were taken as source population.

4.3.2. Study population

All preeclamptic pregnant women attending Chiro, and Gelemso General Hospitals, and all gestational age matched healthy controls, which met the inclusion criteria during the study period, were included in the study population.

4.4. Eligibility criteria

4.4.1. Inclusion Criteria

All preeclamptic pregnant women more than or equal to 20^{th} week of gestation with blood pressure of ≥ 140/90mmHg on two different measurements made within 4 hours' interval and those who had protein urea >1+ with dipstick in fresh collected random urine sample, who are already admitted and/or newly diagnosed patients.

4.4.2. Exclusion Criteria

Patients having hypertension due to other causes (secondary hypertension) on history, patients having other causes of thrombocytopenia identified on history, patients on anti-platelet drugs identified by history, and patients on anti-inflammatory drugs were excluded from the study.

Study participants who were seriously sick and feel uncomfortable to answer the questions and those who were refusing to participate in the study.

Apparently health controls who do not want to participate in the study were excluded.

4.5. Sample size determination and Sampling technique

4.5.1. Sample size determination

The required sample size was determined using double population proportion formula or comparison of two means with equal sample size;

$$n_1 = n_2 = \frac{(z_{\alpha/2} + z_{\beta})^2 (\sigma_1^2 + \sigma_2^2)}{\Delta^2}$$

Where; $n_1 = n_2$ = sample size, Zα/2 = standard normal value for level of significance (1.96), Z_β = standard normal value for power =80, δ1 = population standard deviation for pre-eclamptic pregnant mothers and δ2 = population standard deviation for normotensive pregnant women, Δ = population mean difference, which means, (μ1- μ2), where μ1= population mean for pre-eclamptic pregnant women and μ2 = population mean for normotensive pregnant women.

Based on these assumptions, the population mean and population standard deviation of platelet count was taken from the comparative cross-sectional study conducted in Lahore, Pakistan(36). Accordingly; δ1= 100.58 and δ2 =70.35, μ1 = 219.43 and μ2 = 254.43 and the final sample size were 97 for pre-eclamptic and 97 for normotensive pregnant women, then a total of **194** study population were recruited based on the following calculation:

$n1=n2= (1.96+0.8)^2 *(100.58)^2+ (70.35)^2/ (\mu1- \mu2)^2 = (219.43-254.43)^{2}$

= 7.6* 10116+4994/ 1225, = **97**.

4.5.2. Sampling Technique

Consecutive sampling technique was used until total sample size of **97** pre-eclamptic and **97** normotensive pregnant women was recruited within the study period.

4.6. Study variables

4.6.1. Dependent Variables

Hematological parameters abnormalities

4.6.2. Independent Variables

Socio-demographic factors: - Age, residence, occupation, educational level

Reproductive history: - blood pressure, gestational age, gravidity, parity, age of first pregnancy

Life style**:** - Obesity, fruit consumption habit, smoking mothers

4.7. Data collection technique

4.7.1. Socio-demographic and clinical data collection

Pre-tested structured questionnaire were used to collect socio-demographic variables and clinical data of the study participants using face to face interview by oriented midwives. Previous medical history was collected by reviewing patient's records using checklists. Data collectors were oriented with the objective of standardizing the data collection instrument and providing them with basic skill of extracting the data both from the log book as well as ANC follow up cards. The questionnaires were arranged after revising different related journals outside and inside the country.

4.8. Specimen Collection, Processing and Laboratory investigations

4.8.1. Blood Sample Collection and Examination

A four milliliters of venous whole blood were collected from the study participants by qualified laboratory technologists by strictly following standard operating procedure (SOPs) using vacutainer tubes (purple-cap) containing 2mg/ml ethylene diamine tetra acetatic acid (K2-EDTA). The collected blood samples were thoroughly mixed to avoid clump and clot formation. Obstetrics history of the study participants (age, gestational age and other related clinical history) were obtained from the medical records using predesigned data collection format. Hematological parameters were determined by using hematology auto analyzer Sysmex XN-550, (Sysmex Corporation, Kobe, Japan) within two hours of blood collection. Hematology analyzer was performed according to the dynamic focusing, flow cytometer (using a semi-conductor laser) and impedance (resistance) technology to improve very low and very high test results. All procedures were conducted according to manufacturers' instruction manual.

A urine specimen was also collected using a clean dry leak proof cup to detect proteinuria for newly diagnosed patients. Proteinuria was detected by Cromatest® Linear URS-10 chemical strip (Linear Chemicals S.L, 08390 Montgat, and Barcelona, Spain), which is a semi-quantitative test.

4.8.2. Statistical analysis and interpretation

All questionnaire and laboratory findings were coded and double-checked for accuracy. After that, the data was entered into Epi-Data version 3.1, cleaned, modified, and exported to a statistical package for social science statistical software version 25 (SPSS- 25) for analysis. Data distribution was checked by Kolmogorov-Smirnov normality test. Comparisons of numerical variables of normally distributed data between the two groups was done by independent sample t-test, and descriptive statistics are presented as mean (±) and standard deviation (SD), while comparison of numerical variables that were not normally distributed or skewed distribution, Mann-Whitney U test was done and descriptive statistics were presented as median or interquartile range (IQR). Receiver Operator Characteristic (ROC) Curve analysis was performed to determine AUC, sensitivity and specificity of a given hematological parameters and for predicting preeclampsia. Crude and adjusted odd ratios (OR) and 95% CI were calculated and multiple logistic regression models were constructed to identify the independent risk factors with hematological abnormalities. For all statistical analysis, $p< 0.05$ was considered as statistically significant.

4.9. Data quality assurance and Management

To assure the quality of the data, all laboratory activities were done strictly following manufacturer's instruction and SOPs and pre-test was done on 5% of sample size at other hospital with similar characteristic of the study hospitals. The quality Control of CBC analyzer was run daily before patient samples were analyzed, and the collected data were checked for validity, completeness, and internal consistency daily. To ensure consistency, the questionnaires were translated into local language, Afaan Oromo and then back into English. The principal investigator was oriented and monitored the data collectors to maintain the quality of the data.

4.10. Operational definitions

Preeclampsia: - refers to the new onset of hypertension and proteinuria or the new onset of hypertension and significant end-organ dysfunction with or without proteinuria after 20 weeks of gestation or postpartum in a previously normotensive patient(47).

Severe preeclampsia: defined as preeclampsia associated with any of the following: severe hypertension (i.e., SBP ≥ 160 mmHg and/ or DBP ≥ 110 mmHg or both), proteinuria ≥ 3+ with fresh urine using dipstick, pulmonary edema, and new onset of cerebral or visual disturbances, epigastric or right upper quadrant pain, and new onset of seizures(1).

Anemia: Anemia is defined as a low red blood cell count, a low hematocrit, or a low hemoglobin concentration. In pregnancy, a hemoglobin concentration of less than 11.0 g/dl (48).

Severe Anemia: - when the hemoglobin concentration of less than 7g/dl.

Thrombocytopenia: defined as when blood platelet count is less than $150x10^9$/L during pregnancy.

Severe thrombocytopenia: when the platelet count is less than 50 $x10^9$/L during pregnancy.

4.11. Ethical consideration

The study was approved by the ethical review board of the Institute of Health, Jimma University. Supporting letters were obtained from those administers of those selected hospitals. Written informed consents were obtained from all study participants after full explanation about the purpose of the study. The respondents were informed of their right to refuse or agree to be part of the study or discontinue their participation whenever they fill the need. Confidentiality of the data was maintained during data collection. Blood sample collection was carried out under aseptic technique by well-trained laboratory technologist.

4.12. Dissemination plan

The results of this study will be submitted to school of medical laboratory sciences, Faculty of Health Sciences, institute of health, Jimma University. Then it will be disseminated to west Hararge zone health department and to other governmental and non- governmental stakeholders. Finally, effort will be made to publish the research on local and international reputable peer journals.

5. RESULTS

5.1. Socio-demographic characteristics of the respondents

The study comprised a total of 194 individuals (97 pregnant women with preeclampsia, and 97 healthy controls). From the total study participants, 117 (91%) and 77 (39.7 %) were urban and rural residents respectively. Housewives accounted for the majority of them 124(63.9%), followed by government employee 34 (17.5%) and merchants 29(14.9%). The study participants' age ranged from 17 to 37 years old with a mean age of 27.09 ± 4.979 for preeclamptic patients and 26.99 ± 4.92 years old for the control groups (table-1). There were no significant variation among the study groups (p= 0.24).

Table 1:-Socio-demographic characteristics of study participants attending at Chiro and Gelemso General Hospitals, West Hararge, Ethiopia from November 15, to Feb 15,2022 (**n = 194**)

Variables	Category	Preeclamptic (97)	Controls (97)	P-value
Age (Mean ± SD)		2 7.09 ± 4.979	26.99 ± 4.92	0.240
Educational status, N (%)	Has no formal education	8(8.25%)	0(0%)	
	Can write and read	43(44.3)	6(6.2)	< 0.001
	Primary school	35(36.1)	28(28.9)	
	Secondary school	9(9.3)	58(59.8)	
	Higher education	2(2.1)	5(5.2)	
Residence, N (%)	Urban	46 (47.4%)	71(73%)	< 0.001
	Rural	51 (52.6)	26(27)	
Occupation, N (%)	House-wife	75(77.3%)	49(51%)	
	Farmer	5(5.2 %)	2(2.06%)	< 0.001
	Merchant	10(10.3%)	19(19.6%)	
	Government employee	6(7.2)	27(28)	
Total	**194**	**97**	**97**	

5.2. Clinical characteristics study participants

As shown in **Table 2**, the study participants ranged in age from 17 to 37 years, with a mean age of 27.09 ± 4.98 years for preeclampsia and 26.99 ± 4.92 for the control groups. The mean of preeclamptic women's body mass index (BMI) was 22.94 ± 0.96, while normotensive women's body mass index was 21.87± 0.69. There was no significant difference (p= 0.199) in the mean of BMI between preeclamptic and normotensive women according to result of independent sample t-test analysis. Between the control and preeclamptic groups, there were significant differences in gestation weeks (GWs), gravidity, and parity ($p<0.05$). The mean systolic and diastolic blood pre ssure of preeclamptic women, and controls were 152.27± 9.67, 98.21 ± 9.27 and 118.05± 7.53, and 83.76 ± 5.20 mmHg, respectively (Table 2). Also, statically significant variation were detected ($p<0.001$).

Table 2: Comparison of clinical characteristics of pregnant women by attending Chiro and Gelemso General Hospitals, West Hararge, Ethiopia from November 15, to Feb 15,2022 (**n=194**)

Variables	**Preeclamptic(n= 97)** **Mean** ± SD	**Controls (n= 97)** **Mean** ± SD	**P-value**
Age of mothers	27.09 ± 4.98	26.99 ± 4.92	0.240
BMI (kg/m^2)	22.94 ± 0.96	21.87 ± 0.69	0.199
GA in weeks	32.44 ± 3.89	34.51 ± 4.14	< 0.001
SBP (mmHg)	152.27±9.67	118.05 ±7.53	< 0.001
DBP (mmHg)	98.21 ± 9.27	83.76 ± 5.20	< 0.001
Parity	1.18 ± 1.24	0.73 ± 0.74	0.025
Gravidity	2.15 ± 1.21	1.73 ± 0.86	0.040

Abbreviations:- *BMI-Body mass index, GA- Gestational week, SBP-Systolic blood pressure, DBP-Diastolic blood pressure, SD- Standard Deviation*

5.3. The magnitude of anemia and thrombocytopenia among study participants

From the total of 194 study participants, 153 study participants were not anemic, and 41(42.2%) of them were anemic. Among the total of 97 preeclamptic pregnant women of the study participants, 39(40.21%) were anemic. Preeclamptic pregnant women had anemia to a substantially greater extent (40.21%) as compared with a non-preeclamptic pregnant women 2 (2.06%), (P<0.001).

The present study also revealed that, from a total of study participants 68 (35%) had thrombocytopenia, from which 64 (66%) and 4 (4%), were preeclamptic and normotensive controls, respectively. However, in this study preeclamptic patients had thrombocytopenia with a highest prevalence among study participants, (p = < 0.001).

Table 3: Prevalence of **Anemia** and **Thrombocytopenia** among preeclamptic and normotensive pregnant women attending Chiro and Gelemso General Hospitals, West Hararge, Ethiopia from November 15, to Feb 15,2022 (n=**194**)

Variables	Category	Preeclamptic (No & %)	Normotensive (No & %)	Total (No& %)	P-Value
Anemia	**Yes**	39 (40.21%)	2 (2.06%)	**41 (42.3)**	
Status	**No**	58 (59.79%)	95 (97.94%)	**153**	< 0.001
Thrombocytopenia	**Yes**	64 (66%)	4 (4%)	**68 (70%)**	
Status	**No**	33 (34%)	93 (95.8%)	**126**	< 0.001
Total				**194**	

5.4. Comparison of basic hematological parameters among study participants

In this study, the mean (SD) red blood cell (RBC) count was significantly increased in preeclampsia group (3.96 ± 1.4), as compared to the control groups (3.11 ± 0.66) (p< 0.01). Also the mean of mean corpuscular hemoglobin concentration (MCHC) was 32.86 ± 2.4(Pg.) in preeclampsia groups which demonstrate a slight increment as compared to healthy controls which was 32.2 ± 1.2(Pg.), (p= 0.020). On the other hand, the median value of mean cell volume

(MCV) was decreased 84% (83.1-84.4) in preeclamptic group when compared to healthy pregnant controls 86% (85.6-86.7), (P<0.001).

In this study, the median of red cell distribution width (RDW) was significantly elevated 14.6% (13.99-14.8) in preeclamptic groups when compared to normotensive controls, which was 9.6% (9.58-9.85) (p< 0.001). However, the values of Hemoglobin, Hematocrit and Mean corpuscular hemoglobin were not statistically different between the groups, (p> 0.05).

The result of this study also demonstrated that, white blood cell count has shown significant elevation in women with preeclampsia as compared to the healthy control groups with the mean ± SD of (9.01 ± 2.14) x109/L vs. (6.79 ± 1.3) x109/L, respectively (p<0.001). The absolute neutrophil count was also compared among the study groups and there were a statistically significant variation between the two groups, with the mean ± SD values of (6.17 ± 2.86) x109/L in the preeclamptic groups versus (5.36 ± 0.72) x109/L in healthy control groups (p<0.001).

In this study, we found that platelet count was significantly decreased in preeclamptic patients as compared to normotensive pregnant women 147.1± 86.4 (x109/L) vs. 248.22 ± 62 (x109/L),(p< 0.001). However, mean platelet volume (MPV), platelet distribution width (PDW) and the median value of platelet large cell-ratio (PLC-R) was elevated in pregnant women with preeclampsia as compared to healthy controls (p <0.001). The median of platelet large cell ratio (P-LCR) was significantly higher in preeclamptic women 28% (27.4-29.1) as compared to the control groups 24% (23.7-24.62).

This study revealed statistically significant variation between the study groups, (P<0.001). Besides, the mean value of mean platelet volume (MPV) and platelet distribution width (PDW) in preeclamptic pregnant women were substantially greater (11.12 ±1.4) fL and (13.7 ± 1.7) %, as compared to normotensive healthy control groups (9.03 ±0.72) fL and (10.43± 0.95) %, (P<0.001). ***Table 4***, shown the comparison of some basic hematological parameters among study participants

Table 4: Comparison of RBC, WBC, and Platelet parameters by ***Independent t-test*** among preeclamptic and normotensive pregnant women attending at Chiro and Gelemso General Hospitals, West Hararge, Ethiopia from November 15, to Feb 15,2022 (**n=194**)

Variables	Preeclampsia (n=97) Mean ± SD(Median)	Normotensive (n=97) Mean ± SD (Median)	P-value
RBC($x10^{12}$/L)	3.96 ± 1.4	3.11 ± 0.66	**< 0.001**
HGB (g/dl)	11.2 ± 3.5	11.88 ± 0.62	**0.059**
HCT (%)	36.1 ± 11.66	35.62 ± 2.44	**0.700**
MCV(fL)	84(83.1-84.4)	86(85.6-86.7)	**< 0.001**
MCH (Pg.)	27.89 ± 5.73	27.65± 0.92	**0.682**
MCHC (g/dl)	32.86 ± 2.4	32.2 ± 1.20	**0.020**
RDW (%)	14.6 (13.99-14.8)	9.6(9.58-9.85)	**< 0.001**
WBC ($x10^9$/l)	9.01 ± 2.14	6.79 ± 1.3	**< 0.001**
ANC ($x10^9$/l)	6.17 ± 2.86	5.36 ± 0.72	**< 0.001**
Plt(x109/L)	147.1 ± 86.4	248.22 ± 62	**< 0.001**
PLCR (%)	28(27.4-29.1)	24(23.7-24.62)	**< 0.001**
MPV (fL)	11.12± 1.4	9.03± 0.72	**< 0.001**
PDW (%)	13.7± 1.7	10.43± 0.95	**< 0.001**

Abbreviations*:-RBC- Red blood cell, HGB- Hemoglobin, HCT- Hematocrit, MCV- Mean corpuscular volume, MCH- Mean Corpuscular Hemoglobin, MCHC- Mean Corpuscular Hemoglobin Concentration, RDW- Red Cell Distribution Width, WBC- White blood Cell, ANC- Absolute Neutrophil Count, Plt-Platelet, PLCR- Platelet Large Cell Ratio, MPV- Mean Platelet Volume, PDW-Platelet Distribution Width*

5.5. Comparison of Some hematological parameters based on their severity

As the result revealed in **Table 5**, the mean platelet count in severe preeclampsia (**121.24 ± 103.65**) x109/L were significantly lower as compared to mild preeclampsia (161 ± 72.6) $x10^9$/L, (P= 0.030), whereas, the mean value of MPV (11.84 ± 1.26) fL and PDW (15.1 ± 1.12) % were elevated in severe PE than mild cases (10.73 ± 1.3) fL vs. (12.93 ± 1.4) %, respectively (P< 0.05). Besides, in present study, the median value of RDW **15.2%** (14.29-16.0) in severe

preeclampsia were significantly elevated as compared to the mild PE, **14.2%** (13.58-14.4) ($p<0.05$). Moreover, in current study the mean value of RBC were expressively increased in severe preeclampsia (4.38 ± 1.4) $x10^{12}$/L as compared to mild preeclampsia (3.73 ± 1.4) $x10^{12}$/L, (P = 0.029). Similarly, the median of MCV **84.3** %(82.9-85.3) in severe case of preeclampsia were i**ncreased** when compared to the mild cases **83 %**(82.8-84.4), but does not show significant difference between the study groups (P= 0.489).

The present study also showed that, the mean value of WBC count in mild and severe preeclamptic pregnant women were (8.17 ± 1.78) $x10^9$/L, versus (10.17 ± 1.7) $x10^9$/L, respectively ($p < 0.001$). Besides, the mean of ANC also demonstrated that, an increase in severe preeclamptic groups (7.89 ± 0.15) $x10^9$/L, in comparison with mild cases (5.58 ± 0.2) $x10^9$/L, (p = 0.006). The comparison of some hematological parameters with their severity were summarized and presented in table 5.

Table 5 - Comparison of some hematological parameters between mild and severe preeclamptic pregnant women attending Chiro and Gelemso general Hospitals, West Hararge, Ethiopia from November 15, to Feb 15, 2022 **(n=97**)

Variables	**Mild (n=63)** **Mean ± SD**	**Severe (n=34)** **Mean ± SD**	**P-value**
RBC($x10^{12}$/L)	3.73± 1.4	4.38 ± 1.4	0.029
Hb(g/dl)	11± 3.9	11.5± 2.65	0.497
MCV (%)	83(82.8-84.4)	84.3(82.9-85.3)	0.489
MCHC(g/dl)	32.5 ± 2	33.6 ± 2.9	0.032
RDW (%)	14.2 (13.58-14.4)	15.2 (14.29-16)	0.007
Plt ($x10^3$/L)	161 ± 72.6	121.24 ± 103.65	0.030
MPV(fL)	10.73 ± 1.3	11.84 ± 1.26	0.002
PDW (%)	12.93 ± 1.4	15.1 ± 1.12	<0.001
PLCR (%)	26.2 (25.8-27.2)	31.5(29.6-33.2)	<0.001
WBC($x10^9$/l)	8.17 ± 1.78	10.17 ± 1.7	= 0.001
ANC ($x10^9$/l)	5.58 ± 0.2	7.89 ± 0.15	=0.006

5.6. Diagnostic Performance of some hematological parameters Using ROC curve analysis

The diagnostic values such as AUC, cut-off value, sensitivity, and specificity were determined for some hematological parameters that showed significant differences between preeclamptic and the control groups using Receiver Operator Characteristic (ROC) curve analysis. Accordingly, the result of ROC curve analysis showed that, red cell distribution width (RDW) had the largest AUC (**0.690**: 95% CI; 0.529-0.771) and can distinguish preeclamptic patients from normal pregnant women at a cut-off value ≥14.1 with a sensitivity of 50.2% and specificity of 82.6%. As a result of current study, RBC had the second largest AUC (**0.663**: 95%CI; 0.542-0.783) and might differentiate preeclamptic patients from normotensive pregnant women at a cut-off value of ≥3.2 with a sensitivity of 48.6% and specificity of 91.2%.

Classifiers that produce curves closer to the top-left corner perform better. As shown in Figure 1, due to their large AUC, red cell distribution width (RDW) and red blood cells (RBC) was better predictive and diagnostic marker of preeclampsia.

Table 6 -Result of ROC curve analysis of RBC, WBC, and Platelet parameters among Preeclamptic pregnant women attending at Chiro and Gelemso General Hospitals, West Hararge Ethiopia from Nov15, to Feb 15,2022 (**n =97**)

Test Result Variable(s)	Area	Std. Error	Cut off point	Sensitivity (%)	Specificity (%)	p-value	Asymptotic 95% CI	
							LB	UB
RBC	0.663	.061	≥3.2	48.6	91.2	0.008	0.542	0.783
MCV	0.544	.064	≥82.4	44.8	86.8	0.477	0.418	0.670
MCHC	0.650	.058	≥32.6	45.3	79.4	0.002	0.576	0.803
RDW (%)	0.690	.062	≥14.1	50.2	82.6	0.015	0.529	0.771
WBC	0.854	0.044	≥ 8.62	71.5	89.2	< 0.001	0.745	0.916
ANC	0.619	0.057	≥ 6.2	46.9	75.6	0.056	0.507	0.730
MPV (fL)	0.728	0.055	≥10.98	80.1	84.8	< 0.001	0.621	0.835
PDW (%)	0.839	0.042	≥13.4	86.2	78.4	< 0.001	0.757	0.923
PLCR (%)	0.724	0.055	≥27.5	56.8	74.8	< 0.001	0.616	0.833

***Abbreviations**: - Std- Standard, LB- Lower Bound, UP- Upper Bound*

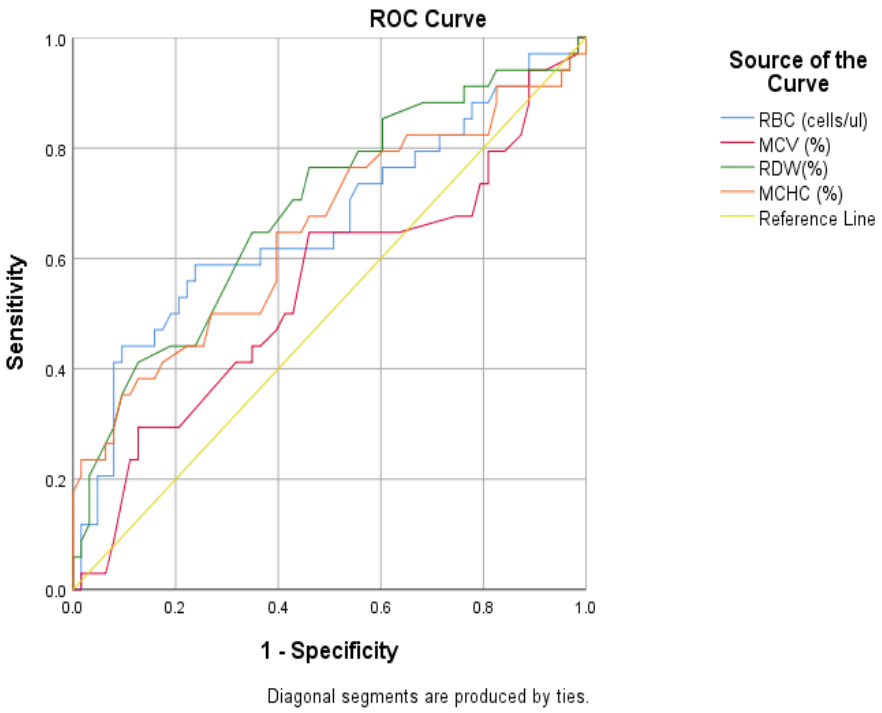

Figure 1- Receiver operator characteristic (ROC) curve analysis for RBC, MCV, RDW, and MCHC among preeclamptic pregnant women attending at Chiro and Gelemso General Hospitals, West Hararge, Ethiopia from November 15, to Feb 15, 2022 **(n=97)**

The result of ROC analysis indicates that, both WBC and ANC could be used as a marker for the diagnosis of preeclampsia with a sensitivity of 71.5% and 46.9% and a specificity of 89.2% and 75.6% at cut-off values of ≥8.62 and ≥6.2 respectively. Besides, the ROC curve analysis demonstrates that, WBC had the highest AUC (0.831, CI; 0.745-0.916), showing that, it is the best parameter which can help distinguish preeclamptic patients from normotensive controls.

Table 6 and **Figure 2** demonstrated that, both white blood cell, and absolute neutrophil count should be used as diagnostic criteria for the presence of preeclampsia because of its high AUC, as both values closed to the threshold value (cut off value). Therefore, both parameters can be used as indicator for the severity and diagnostic marker for preeclampsia.

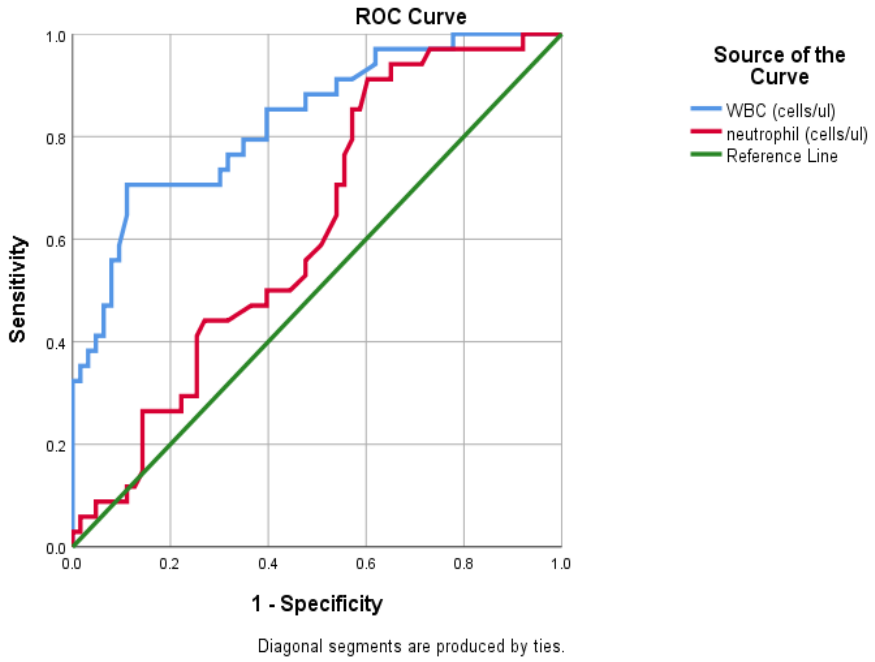

Figure 2: Receiver operator characteristic (ROC) curve analysis for WBC and Absolute neutrophil counts among preeclamptic pregnant women attending at Chiro and Gelemso General Hospitals, West Hararge, Ethiopia from November 15, to Feb 15, 2022 **(n=97)**

The diagnostic values of platelet parameters showed significant difference between the preeclamptic and Control groups. As a result of ROC curve analysis, platelet distribution width (PDW) had the largest AUC (0.839: 95% CI; 0.757-0.923) and can distinguish preeclamptic patients from normotensive pregnant women at a cut-off value of ≥ 13.4 with a sensitivity of 86.2%, and specificity of 78.4%. The values of mean platelet volume (MPV) and platelet to large cell ratio (P-LCR) were also indicated as a marker for the diagnosis of preeclampsia with sensitivity of 80.1%, 56.8 % and specificity of 84.8%, 74.8% at cut-off values of ≥10.98 fL and ≥27.5% respectively.

As depicted in the **figure 3**, the receiver-operating characteristic (ROC) curve is a plot of sensitivity on the *y* axis against (1−specificity) on the *x* axis for varying values of the threshold (cutoff) points ranged from ≥13.4 to ≥ 27.5. This indicated that as cutoff points increased, the sensitivity of the test result that detects the severity of preeclamptic women (diseased group) decreased. As can be shown in **table 6**, PDW had the highest sensitivity (86.2%), means that

there were few false negative results, and thus fewer cases of preeclamptic women were missed, and the reverse of this was true. It is possible to conclude that, platelet distribution width at the cutoff value **≥13.4%** (AUC= 0.839) was the best predictive marker for evaluation of the severity of preeclamptic women as it closed to the threshold value to the left margin of the y-axis.

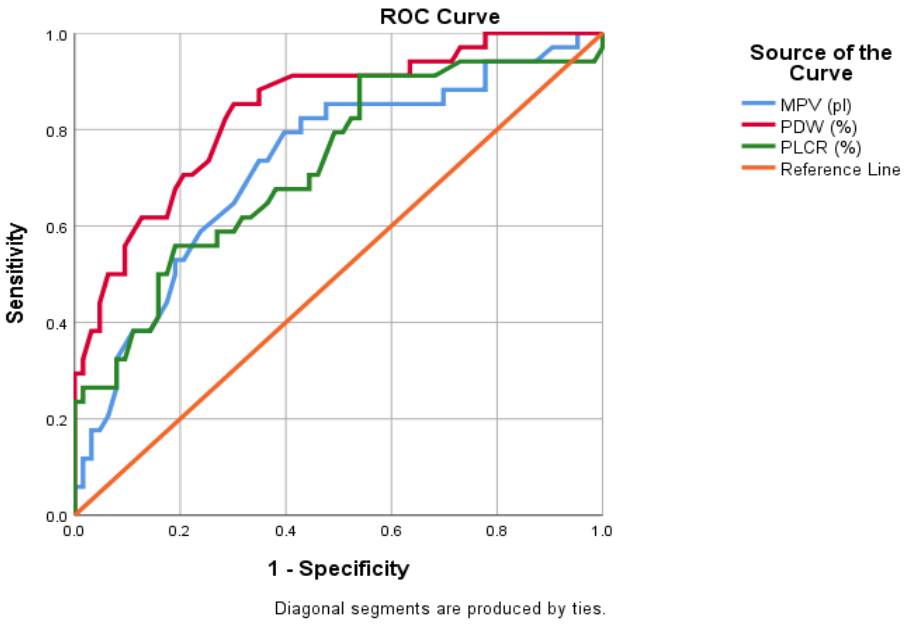

Figure 3 Receiver operator characteristic (ROC) curve analysis for MPV, PDW and P-LCR among preeclamptic pregnant women attending at Chiro and Gelemso General Hospitals, West Hararge, Ethiopia from November 15, to Feb 15, 2022 (n=97)

5.7. Factor associated with Anemia using univariate and multivariate analysis

For six variables pairwise binary logistic regression was done and three variables having p-value less than 0.25 were candidates for multiple logistic regression. After computing multiple binary logistic regression variables having p-value less than 0.05 with 95% CI of adjusted odds ratio used to declare statistical significance. Accordingly, those variables which were candidate for multiple logistic regressions were not having association with anemia.

Table-7 Factor associated with Anemia using bivariate and multivariate analysis of pregnant women attending at Chiro and Gelemso General Hospitals, West Hararge, Ethiopia from November 15, to Feb 15,2022 **(n = 97)**

Variables List	Category	Anemia Status		Bivariate LR		Multivariate LR		
		Yes	No	COR	P-Value	AOR	(95% CI)	p-value
Educational Status of Mothers	No formal education	25	19	2.14	**0.026**	0.698	(0.128-3.817)	0.679
	Can write & read							
	Primary	7	28	1.35	0.999	2.549	(0.460-14.120)	0.284
	Secondary	4	7	1.28	0.999	1.752	(0.198-15.527)	0.614
	Higher Education	3	4	1.00			1.00	
Residence	Urban	19	23	1.00	0.99			
	Rural	20	31	1.01				
Occupation	House wife	30	42	0.53	0.505	0.844	(0.125-5.725)	0.863
	Farmer	5	3	0.24	**0.179**	0.349	(0.33-3.646)	0.379
	Merchant	2	8	0.93	0.949	1.101	(0.109-11.111)	0.935
	Gov't employee	2	5	1.00			1.00	
Parity	Null parity	13	24	1.00				
	> 1 parity	26	34	0.66	0.339			
BMI	18-24.99	30	50	1.00			1.00	
	≥ 25	10	7	0.42	**0.111**	0.399	(0.123-1.298)	0.127
Age of Mothers	18-25	16	23	1.00				
	26-30			1.22	0.686			
		12	21					
	>30			0.75	0.584			
		11	14					

6. DISCUSSION

Preeclampsia is a multi-system disorder which is characterized by the new onset of hypertension after 20th week of gestation. Despite extensive research efforts, the origin and pathogenesis of preeclampsia remain a mystery. There are currently no tests available for the clinical diagnosis of preeclampsia that is based on its etiopathogenesis. Similarly, no scientific method exists to determine the chance of negative outcomes for mothers who present with simple preeclampsia (42).

In the current study, the mean age of cases was 27.09 ± 4.98 which is somehow greater than that of control groups 26.99 ± 4.92 (ranged from 17-37). The current study was consistent with the study conducted in India (49).This study was different from the study conducted in Addis Ababa, found that the average age of the patients was lower than that of the control groups(50, 51). This discrepancy could be due the number of people who were participated in the study.

In this study, about 117 (91%) of the 194 study participants came from urban areas, while 77 (39.7 %) came from rural areas. Furthermore, around 6.2 % had no formal education. About 77 of 97 preeclamptic women (79.4%) can read and write. On the other hand all controls group encountered in the study had formal education. Consistent study reported from Northwest and Omo district southern part of Ethiopia(52, 53). The statistical analysis also confirmed that there was a significant difference between cases, and control groups in terms of their educational level. With regards to their occupation, majority of mothers were housewives accounted for about 124(63.9%), followed by government employee 34 (17.5%) and merchants 29(14.9). The study was consistent with report from Addis Ababa(50), and Gedeo Zone southern part of Ethiopia(54).

In current study the mean of preeclamptic women's body mass index (22.94 ± 0.96) were slightly higher than normotensive women's (21.87 ± 0.69). However, this relationship was not show significant variation among the study groups. This study was consistent with the study conducted in Iran(55). The mean age of gestational week of severe preeclamptic women were lower (32.44) than mild preeclamptic groups (34.51). The result of this study showed statistical significance. This finding was in line with the studies conducted in Ethiopia (56, 57).

According to the current study of independent sample t-test, the mean value of systolic (152.27 ± 9.67, 118.05 ±7.53) mmHg and diastolic (98.21 ± 9.27, 83.76 ± 5.20) mmHg blood pressure among the study groups were demonstrate significantly variations. According to the current finding, preeclampsia and hypertension are directly correlated, meaning that as the condition worsens, and so does preeclampsia. This result is supported by previous studies (55, 58).

In current study, the mean of RBC was found to be elevated in preeclamptic pregnant women as compared to normotensive healthy controls. Additionally, compared to mild instances and healthy pregnant controls, the value of RDW showed an increase in severe preeclampsia patients. It has been demonstrated that an increments of RDW is a condition referred to as anisocytosis, are linked to inflammation in the general population. This study was supported by different previous studies (59-61). In contrast to the present study, the study conducted in Sudan found that, RDW levels were not associated with the presence or severity of preeclampsia(62).

In this study, the value of MCV 84% (83.1-84.4) in preeclamptic pregnant women was decreased as compared to normotensive healthy controls, 86% (85.6-86.7). But, it was not show statistically significant difference between the study groups. This study was supported by previous studies (63, 64). In contrast to this study most of the studies, showed an increase MCV in preeclamptic patients (15, 65). The discrepancy between the literatures may be caused by the use of various automated hematology analyzers and the conditions of the study participants, including their use of medications, level of exercise, menstrual cycle, diet, and other factors that may have an impact on the test findings.

The ROC curve analysis in current study demonstrates that, red cell distribution width had the largest AUC (0.690), indicating that it is the best RBC parameter to predict the presence and the severity of preeclampsia, and used to differentiate preeclamptic women from the control groups. The finding of this study was consistent with previous research from Sudan and Turkey, which found that red cell distribution width were the best red blood cell indices for assessing the severity of preeclamptic women (55, 66).

In this study, there was statistically significant elevation of WBC and absolute neutrophil count in preeclamptic women as compared to the control groups. This study was supported by the previous studies (42, 66-68). The present study result also agreed with previous studies which revealed that an increased values in severe preeclampsia as compared to normotensive control

groups(67, 69). In contrast to this finding, no significant differences observed between mild preeclampsia and healthy controls(69). Both the average white blood cell and absolute neutrophil counts were markedly increased in patients with mild to severe preeclampsia. Additionally, there were statistically significant differences between the groups with mild and severe preeclampsia.

There were significant differences in the diagnostic value of white blood cells and absolute neutrophil counts between the preeclamptic and control groups. The ROC curve analysis result showed that both parameters were used as diagnostic markers, with sensitivity of 71.5 % and 46.9 %, and specificity of 89.2 % and 75.6 % at cut-off values of 8.62 $x10^9$/ L and 6.2 $x10^9$/ L, respectively. The diagnostic value of white blood cells, on the other hand, had a high AUC (0.831, CI; 0.745-0.916), making it the best predictive parameter for distinguishing preeclamptic patients from normal pregnant women. A similar report from previous studies were support our finding(38, 70).

The present study result showed that, there were statistically significant difference between preeclamptic women and the control groups in platelet count, MPV, P-LCR, and PDW. Platelet count (147.1 ± 86.4) $x10^9$/L was lower in women with preeclampsia as compared to the normotensive (248.22 ± 62) $x10^9$/L pregnant women, whereas, the values of MPV (11.12± 1.4), fL P-LCR 28 %(27.4-29.1) and PDW (13.7± 1.7) were significantly increased when compared to normotensive controls (9.03± 0.72) fL, 24 %(23.7-24.62) and (10.43± 0.95) %, respectively. This study was in line with previous studies which demonstrate in preeclamptic cases there were higher increments in platelet indices, while a significant decrease in platelet count as compared to normal controls (8, 9, 27, 71). In this study, severe preeclampsia had a significantly lower platelet count as compared to mild PE, while, MPV, PDW and P-LCR were elevated as the disease severity progresses. This study was supported by different studies (9, 72-74). The increase in mean platelet volume (MPV)fL, and platelet distribution width (PDW)% in mild and severe preeclampsia most likely points out increased platelet turn over which could substantiate the evidence that platelet survival time is decreased, resulting in the increased destruction of platelets (75).

The increased platelet turnover following a reduction in platelet survival time brought on by an increase in PLT activation, which indicates high bone marrow activity, could account for the

preeclamptic group's elevated P-LCR levels (42). This study is consistent with the studies conducted in Sudan(71), south Korea republic (73) and Turkey(8). Preeclampsia affects multiple organs, making it challenging to identify severity markers for its development. In this study, the MPV, P-LCR and PDW in pregnant women with preeclampsia presented a greater increase with the presence and disease severity, and they can be used as a best predictor and severity marker for the disease. This study also supported by the study conducted in Turkey (76), and Ethiopia (72).

The ROC curve analysis showed that platelet distribution width (PDW) had the largest AUC (0.839: 95% CI; 0.757-0.923) and can differentiate preeclamptic patients from normotensive pregnant women at a cut-off value of ≥ 13.4 with a sensitivity of 80.2%, and specificity of 84.6.1%. The mean platelet volume (MPV) and platelet to large cell ratio (P-LCR) were also indicated as a marker for the diagnosis of preeclampsia at cut-off values of ≥10.98 fL and ≥27.5% respectively. As a result of the presence of the highest AUC, the platelet distribution width is the best indicator for predicting preeclamptic patients and distinguishing the severe preeclamptic patients from mild and/or normotensive pregnant women. Identical report from Southern part of Ethiopia, and others were reported that platelet indices, including mean platelet volume, and platelet distribution width have been identified as the best markers for predicting preeclampsia severity in pregnant women (9, 72, 73).

According to the present study, the mean of platelet count in severe preeclamptic pregnant women were decreased when compared to mild preeclampsia, however, the mean value of MPV (fL) and PDW (%) were elevated in severe preeclampsia as compared with mild preeclamptic groups. Besides, in this study the mean of RDW were elevated in the presence and as the severity of the disease progresses. Statistically significant differences were observed between the study groups. This study was in line with the studies (59, 60, 77).

6.1. Limitation of the study

- ✓ The fact that a few institution based study, which limits the generalizability of the findings, is a major limitation of the study.
- ✓ Another constraint that encountered was the small sample size, which may restrict the study's statistical power.
- ✓ Furthermore, the study's cross-sectional design prevents us from establishing a cause-and-effect relationship.
- ✓ Resource constraints were a key issue at the time of sample collection, limiting the number of participants in the sample. As a result, only Chiro and Gelemso hospitals were considered for the study area.

7. CONCLUSION AND RECOMMENDATION

7.1. Conclusion

. In conclusion, the majority of hematological parameters in the study between preeclamptic and normotensive pregnant women revealed statistically significant variations. But, there was no significant difference observed in the values of hemoglobin (Hb), Mean corpuscular hemoglobin (MCH), hematocrit (Hct) between preeclampsia and control group.

From the standing point of ROC curve analysis, the red cell distribution width, Red blood Cell, MCHC, white blood cell count, platelet distribution width, platelet large cell ratio, and mean platelet volume have been found as potential predictors of preeclampsia and its severity.

However, more research evaluating hematological parameters in preeclamptic women is needed to clarify the role of red blood cell, white blood cell, and platelet indices in PE development and severity. A large-scale longitudinal study should be pivotal in a wide geographic area to evaluate whether it is possible to predict pre-eclampsia severity and to identify potential markers for pre-eclampsia prediction.

7.2. Recommendation

Based on the finding of the current study, the following recommendations are forwarded.

Chiro and Gelemso General Hospitals should incorporate evaluation of the hematological parameters of pregnant women as part of their ANC follow up.

For clinicians more emphasis should be given for the evaluation of red blood cell indices, (RDW and MCV), total white blood cell, absolute neutrophil counts, and platelet indices (MPV, PDW and P-LCR) as an alternative diagnostic tool for preeclampsia in pregnant women.

For researchers further multicenter prospective cohort studies with large sample size which could evaluate other blood parameters including Liver function tests (to evaluate whether the disease gets complicated or not) at various gestational ages of pregnancy are required to confirm the role of these parameters in diagnosing and predicting the presence and severity of preeclampsia.

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ANNEXES

Annex-I: Structured Questionnaires

Structured questionnaires (English Version)

Data Collection

Pre-tested Structured questionnaire was used to collect Data on the socio-demographic and associated factors of the study participants using face to face interview by oriented midwives and previous medical history was collected by reviewing patient's records using checklists.

Title of the study: Hematological parameters abnormalities and associated factors among pre-eclamptic and normotensive pregnant mothers at Chiro and Gelemso General Hospitals, West Hararge zone, Eastern Ethiopia.

Introduction to the study: - This study was aimed to assess hematological parameter abnormalities among preeclamptic and normotensive pregnant mothers, and will hopefully help the clinicians to early diagnose and manage the complication of the disease outcomes, and support in order to inform policymakers and guide strategies for early detection and appropriate management of these conditions and bridges the gap of information concerning the study locally in current study area, in the region and also in the country.

The participation in this study was based on your voluntary and you have the right to refuse to participate in the study, and the confidentiality of the information gathered from you will be kept and used for this study only. The result of the laboratory findings will be communicated to your gynecologists, midwives or your care givers.

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SCHOOL OF MEDICAL LABORATORY SCIENCE

CATEGORY OF HEAMATOLOGY & IMMUNOHEAMATOLOGY

Questionnaire: to assess the prevalence Hematological parameters and associated factors among Pre-eclamptic and normotensive pregnant women at Chiro and Gelemso General Hospitals, west Hararge Zone, 2022.

Direction: -Please encircle the number of your answer or correctly fill in the black space provided for open ended questioners. Thank you for your commitment!

Code of the participants_____

Part – 1:- Socio-demographic Characteristics of the study participants.

Code	**Study variables**	**Possible responses of the participants**	**Remark**
101	Age	_____ in year	
102	Residence	a. Urban b. Rural	
103	Educational Level	a. Unable to write and read (0) b. Can write and read (1) c. Primary school (2) d. Secondary school (3) e. Higher education (4)	
104	Occupation	a. Student (0) b. House wife (1) c. Farmer (2) d. Merchant (3) e. Government employee (4) Other (specify) _____	

Part-2 Reproductive history of the study participants

Code	Study variables	Possible responses of the participants	Remark
201	Parity (number of Child)	_____	
202	Gravidity (number of Pregnancy)	_____	
203	Maternal age	___in year	
204	Age of first pregnancy	___in year	
205	History of abortion or miscarriage	a. Yes (0) b. No (1)	
206	Multi-fetal gestation in current pregnancy	a. Yes (0) b. No (1)	
212	Gestational age	___in weeks	

Part-3:- Participants Life Style

Code	Study Variables	Possible responses of the participants	Remarks
301	Obesity (BMI)	___ kg/m^2	
302	fruit consumption habit during pregnancy	a. Yes (1) b. No (2)	
303	Folate intake during pregnancy	a.Yes b. No	
304	Iron sulfate intake during pregnancy	a. Yes b. No	

Part-4 Disease condition of the study participants

Code	Study Variables	Possible responses of the participants	Remarks
401	personal history of diabetes	a. Yes (1) b. No (2)	
402	anemia in pregnancy	a. Yes (1) b. No (2)	
403	Mothers on inflammatory and anti-platelet drugs	a Yes (1) b No (2)	
404	urinary tract infection (UTI) in pregnancy	a. Yes (1) b. No (2)	
405	previous history of preeclampsia	a. Yes (1) b. No (2)	
406	Chronic Liver and heart disease	a. Yes (1) b. No (2)	

Annex-II: Laboratory Test Results Form

Participant's unique Number (code no): _____

Serial Number	Variable	Results
	RBC	cells/µl
	HGB	gm/dl
	HCT	%
	MCV	fL
	MCH	Pg.
	MCHC	%
	RDW	%
	WBC	cells/µl
	Neutrophil counts	cells/µl
	Platelet count	cells/µl
	MPV	fL
	PDW	%
	PLCR	%

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CATEGORY OF HEAMATOLOGY & IMMUNOHEAMATOLOGY

Questionnaire: to assess the prevalence Hematological parameters and associated factors among Pre-eclamptic and normotensive pregnant mothers at Chiro and Gelemso General Hospitals, west Hararge Zone, 2021.

Direction: -Please encircle the number of your answer or correctly fill in the black space provided for open ended questioners. Thank you for your commitment!

Koodii hirmaatuu _____

Gaaffillee (Questionnaires) varshiinii Afaan Oromoo.

Kutaa 1^{ffaa}: gaaffii Hawaas diinagdee.

Coodii	Gaaffilee qorannoo	Deebi hirmaattonni kennuu danda'an	Yaada
101	Umrii Waggaan	_____	
102	Iddoo jireenyaa	a) Magaala b) Baadiyyaa	
103	Sadarkaan barnoota	a. Dubbisuu fi barreessuu hin danda'u (0) b. Dubbisuu fi barreessuu ni danda'a (1) c. Sadarkaa 1ffaa (2) d. Sadarkaa 2ffaa (3) e. Sadarkaa ol'anaa (4)	
104	Hojii	a. Baratuu (0) b. Haadha manaa(1) c. Qotee bulaa (2) d. Daldaaltuu (3) e. Hojjatuu mootummaa (4) f. Hojjatuu miti mootummaa (5) g. Dafqaan bultuu (6) Kan biraa (ibsi) _____	

105	Haala fuudhaa fi heerumaa	a. Qeenxee (0) b. Kan Heerumte (1) c. Kan irraa du'e (2) d. Kan addaan bahan (3)	

Kutaa 2ffaa. Seena walhormaata hirmaatuu

Coodii	Gaaffilee qorannoo	Deebi hirmaattonni kennuu danda'an	Yaada
201	Lakkoofsa daa'ima deesse	_____	
202	Yeroo meeqa ulfa baatte	_____	
203	Umrii haadhaa	____ waggaan	
204	Umrii ulfa jalqabaa	____ waaggaan	
205	Seena ulfa ofirraa baasuuykn sirra bahuu	a. eeyyen(1) b. lakki (2)	
206	Haala hordoffii da'uumsa duraa	a. kan galmaa'ee (1) b. kan hin galmaa'ini (2)	
207	Ulfi amma garaa qabdu lakkuudhaa	a. eeyyen (1) b. miti (2)	
208	Sadarkaa ji'a ulfaa	1ffaa ___, 2ffaa____, 3ffaa _____	
209	Waggaa itti heerumte	___ waggaan	
210	Umrii ulfaa	___ torbaaniin	

Kutaa-3ffaa:- Haala jireenya Hirmaatuu

Coodii	Gaaffilee qorannoo	Deebi hirmaattonni kennuu danda'an	Yaada
301	Furdina qaamaa (BMI)	_____ kg/m^2	
302	Yeroo ulfaatti amala kuduraa nyaachuu	a. eeyyen (1) b. lakki (2)	
303	Amala sigaaraa xuuxuu	a. Hin xuuxu (1) b. Ni xuuxa (2)	
Kutaa-4ffaa. Rakkina yeroo da'uumsaa Haadhaa fi Daa'ima irra Gahu			
401	Tarsa'uu gadaamessaa	a. eeyyen (1) b. lakki (2)	
402	Daa'ima osoo hin gahin dhalte	a. eeyyen (1) b. lakki (2)	
403	Daa'imni osoo hin dhalatin gadaamessa keesatti du'e jiraa?	a. eeyyen (1) b. lakki (2)	
404	Ulfaatina daa'ima dhalatee	____ graamiidhaan	
405	Gadaamessa keesatti guddinni daa'imaa dhaabatee?	a. eeyyen (1) b. lakki (2)	
405	Torbaan daa'imni itti dhalate	____ Torbaaniin	

Kutaa-5ffaa. Bu'aan qorannoo laaboraatoorii fi seenaan haala Hirmaataa Gaaffiilee kana waliin walitti hidhama

Code	Study Variables	Possible responses of the participants	Remarks
501	Evidence of pre-eclampsia, BP ≥140/90 mmHg, Proteinuria,	a. Yes (1) b. No (2)	
502	family history of hypertension	a. Yes (1) b. No (2)	
503	family history of DM	a. Yes (1) b. No (2)	
504	personal history of diabetes	a. Yes (1) b. No (2)	
505	anemia in pregnancy	a. Yes (1) b. No (2)	
506	Mothers on inflammatory and anti- platelet drugs	a Yes (1) b No (2)	
507	urinary tract infection (UTI) in pregnancy	a. Yes (1) b. No (2)	
508	previous history of preeclampsia	a. Yes (1) b. No (2)	
509	Chronic Liver and heart disease	a. Yes (1) b. No (2)	
510	Blood pressure evidence of severe preeclampsia, BP≥ 160/110, in two occasions 4hrs apart	a. Yes (1) b. No (2) _____/_____mmHg	

Annex-III: Laboratory Procedure - Standard Operating Procedures

Principle of Sysmex XN-550 Hematology analyzer for CBC

The Sysmex XN-550 is multi-parameter quantitative automated hematology analyzer for in vitro diagnostic use in determining whole blood diagnostic parameters. The devices perform hematology analyses based on the hydrodynamically focused impedance measurement, the flow cytometry method (using a semiconductor laser) and the SLS-hemoglobin method.

The device counts and sizes red blood cells (RBC) and platelets (PLT) using hydrodynamic impedance counting (sheath flow DC method). At the same time the hematocrit (HCT) is measured as a ratio of the total RBC volume to whole blood via the RBC pulse height detection method.

Cytometry is used to analyze physiological and chemical characteristics of cells and other biological particles. Flow cytometry is a method used to analyze those cells and particles as they pass through extremely small flow cells.

SPECIMEN:

A. Required specimen

1. Whole blood anticoagulated with a potassium EDTA is preferred.
2. Sodium Citrate may be used when EDTA platelet clumping or platelet satellitism is noted on the EDTA specimen. Platelet counts, immature platelet fraction and WBC counts are the only parameters that may be resulted from the Sodium Citrate specimen. If reporting results from the Sodium Citrate specimen, attach canned comment (Citrated sample. Results may vary from EDTA).

B. Specimen volumes required

1. Optimal draw is a tube drawn to capacity. The collection tube must be filled to a minimum of one-half full for acceptable results.
2. A minimum of 1 mL of whole blood is required for sampler analysis.
3. An EDTA raised bottom microtainer filled above the 250 uL line is adequate. A standard EDTA microtainer must contain 160 uL, though to maintain the proper anticoagulant ratio it must have been filled to the 250 uL line at the time of collection.

C. Unacceptable specimens including those listed below must be redrawn:

1. clotted samples or those containing clots or fibrin strands. All microtainer specimens will be checked for clots prior to sampling by the analyzer.

2. Samples drawn above an IV.

D. Characteristics that may affect test results:

1. Lipemia (may falsely increase Hb)

2. Icterus (may falsely increase Hb)

3. Cold agglutinins (may falsely increase WBC count, MCV and MCHC; may falsely decrease HCT & RBC count)

4. Severe hyponatremia (decreased plasma sodium level) may falsely decrease HCT causing a falsely increased MCHC.

E. Stored Specimen Stability

1. If stored at 4-8^{o}C within 6 hours of collection, EDTA blood samples with normal results may be analyzed up to 48 hours without significant loss of differential stability. The stability may be increased to 72 hours if results do not show a loss of specimen integrity.

2. Slides for a manual differential must be assessed for cellular integrity prior to reporting. If cellular integrity is not intact a manual differential or morphology should not be reported.

3. Sample stability at room temperature is 8 hours. Samples stored at room temperature may exhibit an increase in MCV after 24 hours; this may be minimized by refrigeration.

4. Allow refrigerated samples to come to room temperature for 30 minutes and mix by hand inversion before analysis.

F. Do not place samples on a mechanical rocker.

Constant rocking may cause PLT clumping and alter white cell membranes resulting in false interpretive messages.

REAGENTS / MATERIALS:

Reagent	Volume	Open Expiration
CELLPACK DCL	20L/10 L	60 days
SULFOLYSER	5.0 L	90 days
Lysercell WDF	2 x 4L	90 days
Fluorocell WDF	2 x 42 mL	90 days

Diluents

1. CELLPACK DCL: Whole blood diluent for use in hematology analyzers.

2. CELLPACK DCL Storage:

a. Store at 2^{o}-35^{o}C away from direct sunlight.

b. If frozen, thaw and mix thoroughly before using.

C. CELLPACK DCL is clear and colorless. If it is showing signs of contamination or instability such as cloudiness or discoloration, replace container.

3. CELLPACK DCL Stability:

a. Unopened, it is stable until expiration date printed on the container.

b. Opened, stable for 60 days.

Lysing Reagents

1. Sulfolyser (SLS): Reagent for the automated determination of hemoglobin concentration of blood. Sulfolyser is a lysing reagent that releases the hemoglobin to be measured by the SLS hemoglobin method.

Sulfolyser Storage

I. Store at 1^{o}-30^{o}C away from direct sunlight.

II. Allow the container to equilibrate to environmental temperature (15-30^{o}) prior to use. iii. Replace the reagent if it is showing signs of contamination or instability such as cloudiness or discoloration.

Sulfolyser Stability

I. Unopened, it is stable until expiration date printed on the container.

II. Opened, stable for 60 Days (1.5L) or 90 Days (5L).

Lysercell WDF Storage

I. Store at 2^{o}-35^{o}C away from direct sunlight.

II. Use at an environmental temperature (15-35^{o})

III. Do not use the reagent if it is suspected to have frozen.

IV. Replace the reagent if it is showing signs of contamination or instability such as cloudiness or discoloration

Lysercell WDF Stability

I. Unopened, it is stable until expiration date printed on the container.

II. Opened, 1L stable for 60 days, 2 x 4L stable for 90 days.

Staining Reagents

Fluorocell WDF: Used to stain the leukocytes in diluted and lysed blood samples for determination of differential count in blood.

Cell Clean Auto:

Detergent for fully automated hematology analyzers To be used as a strong alkaline detergent to remove lysing reagents, cellular residuals, and blood proteins remaining in the hydraulics of the analyzer on XN Series/XN-L Series automated hematology analyzers.

Quality Control

Utilizing the Beyond Care Quality Monitor (BCQM) Quality control is performed in order to monitor an analyzer's performance over time. XN-L CHECK is the material used to monitor the performance of the XN-450/550 analyzer. Quality control should be run in accordance with regulatory agency requirements. For the Beyond Care Quality Monitor program, a minimum of 2 levels of controls are needed to be run at least once every 24-hours. It should be noted that for troubleshooting purposes, additional control runs may be necessary. The Beyond Care Quality Monitor program is a toll that will help you determine when troubleshooting is necessary and dynamic screen prompts will guide the end user for the next action. All troubleshooting actions are logged in the Activity Log. (Reference the Beyond Care Quality Monitor User Manual)

A. XN-L CHECK Commercial Controls Instructions for Use

1. Remove vials from refrigerator and allow them to come to room temperature (18-25^{o}C), for approximately 15 minutes.

2. Mix vials according to the package insert accompanying the product until the cell button in the bottom of the vial is completely suspended.

3. Perform a close visual inspection of each vial confirming the cell button is completely removed from the bottom of the vial and cellular elements are uniformly suspended with no aggregates.

Annex- IV: Participants Information Sheets

3.1. Information sheet English version

This information sheet is prepared for those individuals who are willing to participate in the study. The detailed information which is undertaken in the study will explained as follows and is presented after reading the description that informed consent is obtained.

Title of the study: Assessment of hematological parameters and associated factors among pre-eclamptic and normotensive pregnant mothers at Chiro and Gelemso General Hospitals, West Hararge zone, Eastern Ethiopia.

Name of Principal Investigator: Mulualem Gebre Tuke

Email**: mgebre2016@gmail.com**

Phone number: +251911548049 / +251984920943

Address of the Advisors: Mr. Girum Tesfaye (MSc, Assistance professor)

Email: girumtesfaye12@gmail.com. Cell phone: 0920274035

Mr. Dejene Gebre (BSc, MSc)

Email: dejuu10@gmail.com. Cell phone: 0946244535

Purpose of the study: - Assessing the prevalence of Hematological parameters and associated factors among pre-eclamptic and normotensive pregnant mothers has the valuable benefits for the community to early detection and management of pre-eclampsia. Such data are fundamental for the clinicians to give evidence-based intervention, health planers and care givers to guide future policy makers and would serve as baseline information for further studies in the region and at national level.

Procedures: -Following your willingness you are asked to sign a written consent and the following procedures that will be undertaken.

- You will provide us 15 minutes' interview
- Blood sample of about **4**ml is collected for laboratory analysis
- The blood sample will be analyzed for all hematological parameters

Risks and discomforts: -During sample collection we will follow standard operational procedures. The blood drawing may cause minor pain at the site of puncture; however, the pain will no longer appear.

Benefits: - This study will be of benefit to the entire community since its success will aid in proper clinical decision making and treatment of patients. There is no direct financial benefit you get by participating in this study but the test result will be delivered timely and appropriate intervention will be pointed.

Confidentiality: -Any information obtained during this study will be kept confidential. This is assured by avoiding use of any identifier and information will be recorded with code number. We release the result obtained from the study, in the way that avoids any identifier of you and if there is any identifier, there should be signed confirmation of you.

Voluntary participation: The participation in this study is based on your voluntary and you have the right to refuse to participate in the study, and the confidentiality of the information gathered from you will be kept and used for this study only. The result of the laboratory findings will be communicated to your gynecologists, midwives or your care givers. If you do not understand something, you may ask questions now and, in the future, that will be being done, contact the investigator on above address.

Thank you for your co-operation!

4. Ibsa Hirmaattota qo’annootiif gucca guutamu (Afaan Oromoo)

4.1. Ibsa hirmaatootaaf kenamuu kan Afaan Oromoo

Guciin Kun Kan guutamu warren qo’annaa irratti fedhiin hirmaataniif Kan ooluu fi haallii qo’annaa sirritti erga ibsameefii booda Kan guutamu fi Kan mallattaa’udha.

Mata-duree qo’annaa: -Qorannoon bu’aa laaboraatorii parametrii Heematoloojii (Hematological parameter) hadholee ulfaa kan dhiibee dhiibbaa dhiigaa (pre-eclampsia) fi rakkowan isa wajiin wal-fakkatan irratti qorannoon Hospitaalota Harargee lixaa keessatti argaman keessa Hospitaala Chiroo fi Galamso, baha Itoopiyaatti kan gaggeefamu.

Maqaan qorataa: -Mulualam Gabree Tukee

Lak.bilbilaa: - +251911548049 or +251984920943

E. mail: - mgebre2016@gmail.com

Maqaa Gorsootaa: **Mr. Girum Tesfaye (MSc, Assistance professor**)

Email: - girumtesfaye12@gmail.com. Lakk Bilbilaa: 0920274035

Mr. Dejene Gebre (BSc, MSc)

Email: dejuu10@gmail.com. Lakk. Bilbilaaa: - 0946244535

Dhimmi-qo’annichaa: -Bu’aan laboratorii warra haadholle ulfaa dhiibaa dhiigaa (pre-eclampsia) qaban irraa argamu warra karooraa fayyaa baasanii fi gara fuulduraattii warra akka biyyaattii qorannoo Kannan wal-fakatan adeemsisaniif akka bu’uuraattii kan gargaaru ta’a.

Haala adeemsa qo’annichaa: - qo’annoo kana irratti fedhiin hirmaachuu keessan Mallattoo keessaniin nuuf ibsitaaniif ragaalee armaan gadii kanneen nuuf kennitan.

- Gaaffiilee afaaniitiif daqiiqaa 15 waliin turra
- Dhiiga xiqqoo quba gidduu keessan irra ni fudhanna
- Wantootni armaan olii Kun qorannoof Kan barbaachisan tahu ni ibsina.

Sodaa fi miidhaa qabu: -seeraa fi naamusa ogummaa fayyaa hordofuun waan dalagamuuf wanti na sodaachisu hin jiru. Haa tahu malee, dhukkubbiin salphaan yeroo dhiigni fudhatamu namatti dhagahamuu fi kan yeroo xiqqoo turuu ta’ee, garuu miidhaa tokko malee kan badu tahuu isaa kabajaan isiin yadachiisa.

Faayida qo'anniichaa fi kafaaltii hirmaatotaaf godhamu: - qorannoo irratti hirmaachuuf kafaltii kan hin qabnee yoo ta'uu, bu'a qorannoo irraa argamuu fi tajaajila wal 'aansa argachuu ni danda'uu.

Iccitii qo'annichaa: -Firriin qorannoo irraa argaman hundinuu icciitiin kan eeggamaniifi ragaaleen argaman hundinuu maqaa keessaniin osoo hin tahiin lakkoofsa ykn koodii addaatiin kan beekkamaniifi odeeffannoon hundinuu iccitiidhan warra ragaa funaanan biratti kan hafu tahuu isaa isiiniif ibsina.

Mirga fedhidhaan hirmaachuu- qorannoo irratti hirmaachuun fedhii kee qofa tahuu isaa beektee, yeroo barbaadetti qorannoo keessaa bahuu kan dandeessu fi yeroo keessaa baatulee rakkoo tokkoollee kan sirratti hin fidnee fi tajaajila argachuu qabdu hundumaa argachuu kan dandeessu tahuu isaa siif ibsaa, qorannoo kana irratti hirmaachuu keetiif galannii keenya baay'ee guddaadha.

Hirmaanaa keessaniif baay'ee Galatoomi!!

Annex - V: Consent form

1.1 Code of Participant _____

My name is _____ I am here on behalf of Jimma University institute of Health, School of Medical laboratory sciences, Department of clinical laboratory sciences, hematology and immunohematology specialty. I am doing this study for the partial fulfillment of the requirements for master's degree in hematology and immunohematology. The objective of this study is to assess the hematological parameters and associated factors among pre-eclamptic and normotensive pregnant women in Chiro and Gelemso General Hospitals, west Hararge Ethiopia, 2022.

I need your cooperation and honest participation in this study in order to get a valid result that show me real status and help to make intervention; hence, I request to participate honestly. Your participation in the interview and every aspect of the study is completely voluntarily. Your name will not be written in this form and all information that you give me will be kept confidential. You may skip any question that you prefer not to answer, but we would appreciate your cooperation. You may also ask me any question that you need to be clarifying for you if you do not understand them. Only number identifies your responses to our questions, never by name to keep your confidentiality.

Do you agree to participate in this study? 1. Yes 2. No

Signature of the participant _____

Thank you in advance for your cooperation!

1.UunkaaWalii galtee (Afaan Oromoo)

1.1 Lakkofsa addaa (koodii) hirmaatuu _____

Maqaa guutuu hirmaatuu _____

Ani hirmaatuun maqaan koo armaan olitti ibsame kun bu'aa fi miidhaan qorannoon kun narra geesissuu danda'uu erga sirritti natti himame fi miidhaan narra ga'huu danda'ullee baay'ee xiqqaa ta'uu isaa ergan hubadheen booda, saamuda qorannoo laboratoriitiif oolu dhiiga akkan kennuu fi dabalataaniis odeefannoon narraa argaman hunduu icciitiin akka qabaman nattii hiimameera anis itti amannee jira. Akkasumas gaaffilee gaafatamuuf deebii kennuu dhiisuu, hiirmachuu dhabuu fi yeroo barbaadetti qorrannoo kana addaan kutuu akkan danda'uu baree jira. Kana godhuu kiyyaafiis ammas ta'ee fuuldurattis fayyadamummaa tajaajila fayyaa kiyya irratti rakkoon tokkollee akka hin uumamnee huubadhee wan jiruuf, qorannoo kana kessatti hirmaachuu kiyya mallatoodhaan ni mirkanneessa.

Walii galtaniituu 1. Eyyee 2. Mitti

Maqaa hirmaatuu_____ Mallattoo_____ Guyyaa_____

Maqaa qorataa _____ Mallattoo_____Guyyaa_____

Qorannoo kana irratti hirmachuu kessaniif galatooma!

Declaration sheet

Declaration:-

I certify that the thesis "Entitled **Assessment of Hematological parameters abnormalities and associated factors among preeclamptic pregnant women attending Chiro, and Gelemso General Hospitals,"** Oromia Regional States, Ethiopia', Submitted to school of Medical Laboratory sciences, Faculty of Health Sciences, Institute of Health, Jimma University, in partial fulfillments of the requirements for Master of Sciences in Hematology, and Immunohematology which complies with the University regulation and meet accepted standards in terms of originality.

It was carried out by me under the supervision of instructors, Girum Tesfaye (PhD candidate, Assistant professor), and Dejene Gebre (MSc, PhD candidate).

Name of Investigator	Signature	Date
Mulualem Gebre	_____	_____
Name of Advisors		
1. Mr. Girum Tesfaye	_____	_____
2. Mr. Dejene Gebre	_____	_____
Approval of Internal Examiner		
Mr. Gebeyaw Arega	_____	_____
Approval of External Examiner		
Mr. Yaregal Asres	_____	_____