
Addis Ababa University

Addis Ababa University

School of Graduate Studies

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"Clinical Utility of Red Cell Distribution Width in the investigation of Non-Hematological Disorders from May till August 2015, at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: A Case Control Study" and submitted in partial fulfillment of the requirements for the Degree of Master of Science in Clinical Laboratory Science (Hematology and Immunohematology Specialty Track) complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

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Abbreviations

AAU	Addis Ababa University
AKI	Acute Kidney Injury
CBC	Complete blood count
CHD	Chronic Heart Disease
CKD	Chronic Kidney Disease
CI	Confidence interval
CLM	Clinical Laboratory Methods
CRP	C-reactive protein
CRRT	Continuous renal replacement therapy
CV	Coefficient of variation
CVD	Cardiovascular disease
EDTA	Ethylene demine tetraacetatic acid
ESR	Erythrocyte sedimentation rate
HB	Hemoglobin
HD	Hemodialysis
HF	Heart Failure
ICU	Intensive Care Unit
IDA	Iron Deficiency Anemia
LIS	Laboratory Information System
MOH	Ministry of Health
NASH	Nonalcoholic Steatohepatitis
NCD	Non Communicable Disease

NHANES	National Health and Nutrition Examination Survey
MAP	Mean Artery Pressure
MI	Myocardial Infraction
RDW	Red cell distribution width
RR	Risk Ratio
SOFA	Sequential Organ Failure Assessment
SOP	Standard Operating Procedure
TASH	Tikur Anbessa Specialized Hospital

Abstract

Clinical Utility of Red Cell Distribution Width in the investigation of Non-Hematological Disorders from May till August 2015, at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: A Case Control Study.

Background: Red cell distribution width (RDW) is a measurement of the degree of anisocytosis, or the degree of red cell size variability present in a blood sample. RDW has been reported as a significant diagnostic as well as prognostic lab marker for many non-hematological disorders. A study conducted in Addis Ababa showed that RDW was one of the less recognized and underutilized laboratory marker in clinical practice.

Objective: To describe the clinical utility of RDW in the investigation of non hematological disorders at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

Methods: A Case-control and questionnaire based study was conducted at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. A convenient sampling technique was employed and a total sample size of 150 (100 cases and 50 apparently healthy controls) and 100 clinicians were included from May to August, 2015. Cases were adult patients diagnosed with heart, liver and kidney diseases. RDW was determined using Sysmex XT-2000*i* Automated Hematology Analyzer. The data were entered in to Excel spread sheet and imported for analysis to SPSS version 19 software (SPSS INC, Chicago, IL, USA). Frequency, mean distribution, paired t test and chi square was calculated P values less than 0.05 were considered statistically significant.

Result: Half of the clinicians had the Knowledge that elevated RDW could be an indication of non hematological diseases. However, 68% (68/100) of them rated that they rarely or never use RDW in the investigation or follow up of patients having non hematological diseases. Paired t test revealed mean difference of 2.53± 4.3 existed between the cases and control groups with a confidence interval of 1.314-3.76 ($p<0.001$). The association between the three diseases and elevated RDW was found to be statistically significant ($P<0.05$) with 95% confidence interval (0.000-0.030). The clinical laboratory method course for medicine students was rated as inadequate by the majority of them.

Conclusion: RDW's clinical utility by clinicians at TASH in the investigation or follow up of patients with non hematological diseases was insufficient indicating that awareness should be created. Half of the clinicians had the knowledge that elevated RDW could be an indication of

non hematological diseases yet failed to utilize it. Reason behind it is yet to be identified but the habit of utilizing RDW in the investigation of diseases other than anemia should be urged and encouraged.

Key words: RDW, clinical utility, non-hematological disease

1. Introduction

1.1. Background

Red cell distribution width (RDW) is a tool in determination of the degree of red cell size variability in a blood (1). The parameter is measured as a component of the red cell indices in the total/complete blood count (CBC). The normal range of RDW is between 11.5%and 14.5%. RDW is mostly utilized in the differential diagnosis of anemia (2, 3). However, many researchers have reported that RDW is related with elevated morbidity rate in many diseases and established that increased RDW is related with all-cause mortality. Even so, it is used rarely compared with other hematological parameters. It has been reported that RDW is a widely ignored red cell indices despite its relevance in various hematological as well as non hematological diseases (4, 5).

These days, CBC is one of the most frequently requested laboratory tests. The standard CBC test consists of white blood cell (WBC), red blood cell (RBC) and platelet (PLT) counts as well as their morphologic indices. Many researchers have studied the value of these CBC parameters in the forecasting of morbidity and mortality risk (5, 7). High RDW was demonstrated in the case of inflammation and nutritional deficiencies. This particular red cell indices was also predisposed by co morbidities including renal failure (8-10). Prognosis in idiopathic pulmonary arterial hypertension can also be interpreted using RDW results (2, 11) and RDW was also indicated as an independent investigative parameter in heart and cerebrovascular events in the general population and in patients with heart failure, coronary heart disease or peripheral atherosclerosis. In addition, high RDW is closely related with the risk of carotid artery atherosclerosis in patients with hypertension (12-15).

More studies are indicating that RDW is a significant lab marker for the diagnosis and prognosis of patients with hepatitis B, severe sepsis, inflammation, type 2 diabetes mellitus, acute kidney injury, acute coronary syndrome, active Crohn's disease, intestinal tuberculosis, community-acquired pneumonia and acute pancreatitis. The above mentioned researches and others showed that red cell distribution width was significantly increased especially in the mortality of the patients (16-24).

In addition, there are reports indicating the association between RDW and many other disorders such as thrombosis, systemic sclerosis, chronic respiratory disease, inflammatory bowel disease, and general inflammation. It is also indicated in cancer patients such as multiple myeloma (25-29). But this study is only going to focus on heart, liver and kidney diseases. A number of patients suffering from either chronic or acute heart, liver or kidney diseases visit Tikur Anbessa Specialized hospital in order to be diagnosed and treated. Establishing the association between RDW and the three diseases will be vital in improving the health care service in Tikur Anbessa Specialized Hospital, consequently in Ethiopia.

Many blood tests are utilized in the investigation of heart, liver and kidney diseases other than the hematological profiles. Blood tests which aid in the investigation of cardiac diseases includes lipid determinations and C-reactive protein. In fact, clinical examination stays the foundation for the diagnosis and investigation of all kinds of diseases. The clinical examination may then be supplemented by a few types of laboratory tests which might be invasive and non invasive in nature (30).

Blood tests involved in the diagnosis and investigation of kidney diseases include successive serum creatinine evaluation which can offer valuable information to the cause of acute renal failure. The most vital early diagnostic step in the assessment of a patient exhibiting high serum creatinine is to differentiate newly diagnosed chronic kidney disease from acute or sub acute kidney failure because the latter two clinical circumstances may respond to treatment particular to the disease. When investigating patients with suspected chronic kidney disease, serum and urine protein, hemoglobin concentration, iron, B_{12}, and folate must be measured (30). In addition to hemoglobin concentrations, according to many studies, hematological parameters especially red cell indices should be closely monitored.

Investigation and diagnosis in liver disease is mostly supported by the accessibility of specific and sensitive tests of liver injury and function. Distinctive series of blood tests are used for first evaluation of liver disease which include determination of the levels of serum alanine and aspartate aminotransferases, alkaline phosphatase, direct and total serum bilirubin, and albumin and assessing prothrombin time. Pattern of irregularity mostly indicates to hepatocellular versus cholestatic liver disease and will aid to settle on if the disease is acute or chronic and whether cirrhosis and liver failure are indicated (30). Hematological parameters including RDW are also believed to be helpful in the investigation related to different kinds of liver diseases.

Other laboratory tests may be helpful, such as γ-glutamyl transpeptidase to define whether alkaline phosphatase elevations are due to liver disease; hepatitis serology to define the type of viral hepatitis; and autoimmune markers to diagnose primary biliary cirrhosis, sclerosing cholangitis, and autoimmune hepatitis. Liver biopsy is the gold standard in the evaluation of patients with liver disease, particularly in patients with chronic liver diseases. Liver biopsy is more often useful in evaluating the grade and stage of liver damage, in predicting prognosis, and in monitoring response to treatment. RDW is proved to be instrumental in the prognosis and investigation of some of the liver diseases. Potentially, noninvasive means of assessing disease activity such as batteries of blood tests including hematological profile will be used in support to liver biopsy in assessing stage and grade of disease (30).

As there is no research conducted in Ethiopia associating RDW with any of the above listed diseases, this research focused on the existence of association between elevated RDW and the three diseases (heart, liver and kidney). Second, the study also investigates the clinical utility of RDW by clinicians in the investigation of the three diseases just to see how aware the clinicians at Tikur Anbessa Specialized Hospital are of the association. Although RDW is a significant lab marker for the diagnosis and prognosis of patients suffering from non- hematological disorders, it was the most frequently overlooked RBC indices even for hematological disorders according to a study conducted in Ethiopia by Birhaneselassie *et al* (31). This study aimed to prove that clinical significance of RDW and to show its utility in the investigation of non hematological disorders.

1.2. Statement of the problem

High value of RDW had been proven significant as a marker of a variety of critical health problems through researches conducted all over the world. Elevated RDW has a high predictive value for diagnosing a variety of diseases; moreover it suggests vital information for short- and long-term prognosis. Significantly, RDW is now being measured as a strong and independent risk factor for different kinds of diseases indicated in the general population (32).

In a study from the National Health and Nutrition Examination Survey (NHANES), which involved a representative US population, participants with RDW values above the 75th percentile were aggregated in the highest risk category for coronary heart disease (33-37). Other observational studies in selected cohorts of patients with heart disease have reported that RDW predicts all-cause mortality, cardiac morbidity and mortality, and adverse outcome in patients with heart failure (38-40).Furthermore, RDW predicted all-cause mortality and cardiovascular (CV) mortality in 2 population-based studies from NHANES (4).

Research has continuously indicated that elevated RDW could play a role for risk stratification in patients with chronic heart failure. Nevertheless, the prognostic role of RDW in unselected population with acute heart failure (AHF), has not been well recognized. The outcomes of the different studies revealed that RDW is a strong laboratory marker for short- and long-term outcomes in patients with acute exacerbation of Chronic Heart Failure(CHF) and that this prognostic value remains significant. The association between RDW and the long-term outcomes of patients with acute CHF provides investigative data upon which to base risk factors and the association persists regardless of the levels of Hb (40-42). In china, a study indicated possible association between Left ventricular hypertrophy and RDW levels in hypertensive patients since studies conducted all over the world proved that RDW was associated with morbidity and mortality of heart diseases (43,44)

In 1990, CVD accounted for 28% of the world's 50.4 million deaths and 9.7% of the 1.4 billion lost disability-adjusted life years. By 2001, CVD was responsible for 29% of all deaths and 14% of the 1.5 billion lost disability-adjusted life years. When the population is expected to reach 8.2 billion by 2030, 32.5% of all deaths will be the result of CVD. Of these, 14.9% of deaths in men and 13.1% of deaths in women will be due to CHD. Although communicable diseases continue

to be a major cause of death, CVD has appeared to be as an important health concern in the low- and middle-income countries (30).

Sub-Saharan Africa stays mainly in the first phase of the epidemiologic transition, with heart disease rates equaling half of those in high-income nations. Since the early 1990s, life expectancy has been declining by an average of five years mostly due to HIV/AIDS and other chronic diseases, according to the World Bank; life expectancies in the region are the lowest in the world. In the mean time, HIV/AIDS is the number one reason of morbidity in sub- Saharan Africa while heart disease is the third leading killer (30).

New world wide burden of disease estimates for liver cirrhosis, indicate that cirrhosis caused over a million deaths in 2010, with an additional million due to liver cancer and acute hepatitis. Cause-specific mortality data were very sparse for some regions, particularly in Africa, with no significant mortality data for 58/187 countries (45). A study in china showed worse morbidity and mortality rate among patients with liver diseases who had elevated RDW (46). In Nigeria, a finding revealed that patients with hepatitis B had significantly higher RDW values compared with healthy subjects while chronic severe hepatitis B patients had the maximum RDW values among the patients. The most valuable result from the study was that elevated RDW values can serve as an independent predictor of death among HBV-infected patients (16).

RDW , in addition to cardiac and liver diseases , is proved to be associated with kidney diseases among several other diseases. Kidney diseases are increasingly recognized as a worldwide public health issue. The age-standardized global prevalence of CKD stages 1-5 in adults aged 20 and older was 10.4% in men and 11.8% in women. This consisted of 8.6% in men and 9.6% in women in high-income countries, and 10.6% in men and 12.5% in women in low- and middle-income countries. There is now a compelling indication that kidney diseases can be identified using simple laboratory tests, and that RDW is an important negative predictive value in the mortality among patients (47).

In Ethiopia, although published data on the magnitude of the three diseases discussed above is limiting, the country is not an exception regarding epidemiological transition and the magnitude of non-communicable diseases (NCDs) is alarmingly on the rise. This has been confirmed in a large scale multicenter studying which NCDs were attributed as the cause for 35.6% of deaths out of a total of 80,726 registered adult deaths from “INDEPTH Health and Demographic Surveillance System sites in Africa and Asia”, which includes Ethiopia(48). On the other hand,

Even though the RDW is identified as an important lab-marker in many disorders, in Ethiopia, a study conducted by Birhanesellasie *et al* in 2013 showed that RDW was found to be used rarely in contrast with other red cell indices. The research also showed that the utilization of CBC for clinical decision making in the prognosis of patient in Addis Ababa hospitals was insufficient (31).

1.3. Rationale of the study

The aim of this research was to identify if RDW is clinically utilized in the investigation of non hematological disorders by clinicians at Tikur Anbessa Specialized Hospital using a self-administered pre-tested questionnaire. Previously conducted study in Ethiopia found RDW to be the least utilized parameter compared to the other red cell indices in the diagnosis as well as in patient management. However, many studies conducted around the world showed that measurement of RDW is clinically significant for the investigation of non-hematological diseases as well.

RDW is among the several complete blood count (CBC) parameters obtained from automated hematology analyzers using few micro liter of blood in one minute. Although, it is part of the routine CBC result printout, it is little recognized and neglected in its application. Since analysis of RDW is a simple non invasive process to patients, and it takes only a minute, utilizing it as an additional lab marker to investigate non hematological diseases is convenient and extremely helpful to both the patients and the clinicians. It also helps clinicians for following patients' progress while on treatment. This study, in addition to assessing how frequently the parameter is used by our clinicians, it has also aimed to establish RDW as an investigative lab marker for non hematological disorders such as heart, liver and kidney diseases by comparing it with healthy patient's RDW so that RDW is recognized as an important indicative parameter and more frequently utilized for the investigation of patients by clinicians in Ethiopia. TASH being the highest level referral and the largest teaching hospital of the country, introducing the utility of this simple lab marker which has multiple clinical applications with no additional cost, not only improves patient management in this hospital but ultimately do the same in the other health facilities

2. Literature Review

2.1. RDW and Cardiac disease

Mounting body of evidence exists indicating an association between elevated RDW and cardiac related morbidity and mortality. In America, Allen *et al* conducted a prospective study in 2010 and showed RDW as an investigative marker in heart failure. Elevated RDW had a strong, independent relationship with adverse result in the unselected, broadly representative cohort of ambulatory heart failure patients. RDW was a strong forecaster of outcome than numerous frequently used predictors, and has the benefit of already being regularly accessible parameter as part of the automated complete blood count. Increased level of RDW emerged to be a sign of increased inflammation and impaired iron metabolism, a result that suggested the possibility that RDW might provide an integrated measure of these underlying processes in heart failure (40).

A study conducted in Norway by Skjelbakken *et al*, evaluated the relationship between RDW and incidence of myocardial infarction (MI) in a general population. The study was conducted in a relatively homogenous population (99% white), which may bound the generalizability of the outcomes. The findings showed that elevated RDW was related with threat to first-time heart attack episode in the general population. The association was linear and independent of anemia and established heart disease risk feature. Whether RDW is a marker of an underlying pathophysiological condition that leads to risk of MI or just stand for a blameless indicator remains to be established (52).

A systematic review and a meta-analysis conducted in china in 2013 by Huang *et al* showed RDW is of a prognostic significance for patients with Heart Failure (HF). The research indicated that RDW on admission and at discharge, as well as its change during treatment, were of prognostic significance for HF patients. The research also concluded that further studies are needed to uncover the potential mechanisms underlying the associations between a higher RDW and poor prognosis in HF patients. However, the potential prognostic value of RDW should be taken into consideration in the comprehensive management of patients with HF (49).

Another study done in china by Su *et al*, in 2014, also conducted systematic review and meta-analysis of 22 researches enrolling 80,216 participants. The research period lasted between 1 month and 23 years. Elevated RDW indicated, in 15 of the researches done, a major bigger possibility for all-cause mortality in heart disease patients. The meta-analysis indicated that higher RDW levels were associated with higher possibility of death and heart disease events in patients with well-known coronary artery disease (50).

RDW was reported as a more dominant prognostic marker in patients suffering from Congestive Heart Failure than hemoglobin levels in a retrospective study conducted in Tokyo by Dai Y *et al* in 2014. The study went on to explain that RDW may be an earlier indicator of prognosis than Hb as it reflects the early steps in the complex processes that lead to anemia. At the stage of congestive heart failure, red blood cell production is unsuccessful and red blood cells are destroyed, even though Hb stays within the normal value. Hemodynamic changes happening interfere with the measurement of hemoglobin which results in false indication of anemia (43).

Makhoul *et al* in their retrospective study conducted in Israel in 2013 also demonstrated RDW to be a strong self-determining forecaster of mortality and morbidity among patients hospitalized from acute decompensated heart failure. The research concluded that during hospitalization patients with higher RDW level had more adverse clinical outcome (51).

2.2. RDW and Kidney disease

A retrospective study was carried out by Tekce *et al* in Turkey which evaluated RDW in chronic hemodialysis (HD) patients. Their study concluded that in an HD population with sufficient iron stores and without anemia and hypervolemia, the following are indicated: (1) RDW is increased above normal reference range in end stage renal disease patients, especially in the subgroup of patients with inflammation and malnutrition, (2) independent risk factors associated with RDW elevation were HD duration, C- reactive protein (CRP), inter-dialytic weight gain, and albumin levels, (3) RDW was positively correlated with HD duration, inter-dialytic weight gain, and negatively correlated with serum albumin (53).

A recent case-control study done in 2015 by Zhang *et al* in china deduced that RDW may be independently associated with microalbuminuria in patients with newly diagnosed Type 2 diabetes mellitus. RDW could be treated as effective predictive index in the assessment of diabetes nephropathy or diabetes-associated complications (54).

In a cross-sectional study conducted in china by Li Z *et al* in late 2014, RDW was shown as an easy and quick measurable index which can predict early-stage renal function damage in essential hypertensive patients without receiving drug treatment. Significant positive correlation was observed between albumin to creatinine ratio and RDW in hypertensive patients (55).

Oh *et al* in 2012, in Korea conducted a retrospective research on RDW in acute kidney injury patients treated with continuous renal replacement therapy (CRRT). At the beginning of the therapy, RDW level was considerably associated with WBC count, hemoglobin and total

cholesterol. Patients with high RDW levels revealed significantly higher 28-day mortality rates than patients with low RDW levels. RDW level was an independent risk factors for mortality. In conclusion, Elevated RDW might be one of the indicator for death in acute kidney injury patients on treatment in the intensive care unit (20).

2.3. RDW and Liver disease

A retrospective study was carried out in turkey by Cengiz *et al* in 2013 that questioned if increased RDW is an indicating marker of nonalcoholic steatohepatitis (NASH) and fibrotic stage. The study found that patients with NASH had higher RDW values compared with simple steatosis and healthy control groups. Patients with advanced fibrosis had higher RDW values than the mild fibrosis group. They finally concluded that RDW is a new non-invasive marker that can be used to demonstrate the presence of NASH and indicate advanced fibrotic scores (57).

On the other hand, another retrospective study was done in Croatia, Europe, in 2011 by Millic *et al*, which determined the clinical utility of RDW in diagnosing alcoholic and non-alcoholic liver cirrhosis. There were 204 patients in the alcoholic liver cirrhosis group (85%) while non-alcoholic cirrhosis group was composed of 37 patients (15%). In group of alcoholic cirrhosis patients the average RDW was 16.8%. The study didn't find statistically significant difference of RDW between alcoholic and non alcoholic cirrhosis. Moreover they did not prove any statistically significant increase of RDW in relation to severity of disease in group of alcoholic cirrhosis nor in group of patients with non-alcoholic cirrhosis. Their study also showed that RDW had not any clinical value in differentiation of anemia neither in alcoholic and non-alcoholic liver cirrhosis nor in severity of liver disease (58).

In 2015, a study conducted in china by Xu *et al* aimed to prove the association between elevated RDW and liver fibrosis and inflammation due to Hepatitis B infection. The independent variables that establish the severity of liver fibrosis and inflammation were searched. RDW values were observed to be elevated with progressive liver fibrosis and inflammation. After adjustments for other potent predictors, liver fibrosis (moderate-severe) was independently associated with RDW, platelet, and albumin , whereas increased odds ratios of significant inflammation were found for RDW, alanine aminotransferase, albumin, and PLT (56).

In Ethiopia, no study is available assessing the clinical utility of RDW for non-hematological disorders. Moreover, the association between high RDW and non-hematological disorders were

never investigated, necessitating the need for evaluating the clinical utility of this easily obtained simple and yet neglected marker.

3. Objectives

3.1. General Objective

- To describe the clinical utility of RDW in the investigation of non hematological disorders from May- August, 2015 at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

3.2. Specific Objectives

- To determine the clinical utilization of RDW in the investigation of heart, liver and kidney diseases.
- To calculate the mean difference of RDW values between case and control groups.
- To calculate the association between elevated RDW and the non hematological diseases.

3.3. Hypothesis

- RDW is not clinically utilized in the investigation of non hematological diseases

- There is a statistically significant association between elevated RDW and non hematological diseases.

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4. Materials and Methods

4.1. Study Area

Tikur Anbesa Specialized Hospital (TASH), located in the nation's capital Addis Ababa, is Ethiopia's largest referral public hospital. In 1998, Tikur Anbessa Hospital, was given to Addis Ababa University (AAU) by the Ministry of Health (MoH) to serve the faculty as a main teaching hospital. The hospital provides a tertiary level referral treatment and is open 24 hours for emergency services. TASH offers diagnosis and treatment for approximately 370,000-400,000 patients a year in its specialty clinics including hematology, renal, cardiac and gastroenterology units. The hospital has 800 beds, with 130 specialists, 50 non-teaching doctors, more than 350 residents. The emergency department sees around 80,000 patients a year.

The main hematology laboratory test menu includes: ESR or erythrocyte sedimentation rate, Blood film, CBC and coagulation tests. Approximately from two hundred fifty up to three hundred samples per day come to hematology laboratory for different investigations. This study site is selected to be at TASH because of (1) the felt responsibility of the hospital to produce quality doctors as it is a university hospital. (2)It is also a practical attachment site for medical laboratory science students. (3) The hospital has different types of automated hematology analyzers both with 3- and 5-part differential counts. (4) Since it is one of the largest referral hospitals, patient diversity is also high. (59).

4.2. Study Period

The study period of this research was from May- August, 2015.

4.3. Study design

A Case-control, questionnaire and laboratory based study was conducted at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

4.4. Population

4.4.1. Source Population

The source populations were all the patients who came to Tikur Anbessa Specialized Hospital to get medical treatment for heart, liver and kidney disease from May- August, 2015 and all the clinicians currently working at internal medicine and pediatrics department at Tikur Anbessa Specialized Hospital.

4.4.2. Study Population

The study populations were adult patients diagnosed with heart, liver and kidney diseases from May- August, 2015. All clinicians actively working in internal medicine and pediatrics department who volunteered to fill a self-administered questionnaire which assessed the clinical utility of RDW.

4.4.3. Controls

Apparently healthy individuals which are age and sex matched with the study population were used for comparison. These are volunteering staffs of TASH as well as staffs and students from department of medical laboratory sciences

4.5. Inclusion and Exclusion criteria

4.5.1. Inclusion Criteria

- Patients of heart, liver and kidney disease above the age of 18 for whom CBC was requested for analysis and were willing to participate in the study.
- For the clinical utility study, all volunteering clinicians in internal medicine and pediatrics department of the hospital were included
- For controls: apparently healthy staff and students who were willing to take part in the study.

4.5.2. Exclusion Criteria

- Patients with cardiac, liver and kidney diseases who were anemic.

4.6. Study Variable

4.6.1. Dependent Variable

- RDW
- Clinical utility

4.6.2. Independent Variable

- Socio demographic information (For case and control Sex& Age : Specialty and service of year for clinicians …).
- Non hematological disorders (Cardiac, Renal and liver diseases)

$$n = (\frac{r+1}{r})\frac{\pm^{2}(Z \quad + Z_{\sim/2})^{2}}{(d\text{ifference})^{2}}$$

$$n = (1.5)\frac{10^{2}(7.84)}{(5)^{2}} = (1.5)2^{2}(7.84) = 47$$

4.7.3. Data Collection procedure

Patients who came to Tikur Anbessa Specialized Hospital during the study period who fulfill the inclusion criteria and also apparently healthy study participants RDW were analyzed using SYSMEX 2000i hematological analyzer and recorded to establish the difference in mean RDW between patients and controls. While clinician's experience and frequency of utilizing the RDW results in order to diagnose non hematological disorders was asked through a self- administered questionnaire. The self- administered questionnaire was sent to department of internal medicine at the Tikur Anbessa Specialized Hospital. Clinicians such as general practitioners (GPs), internists, and pediatricians were asked to collaborate and provide their feedback. The data involving clinicians' feedback was collected using a questionnaire and patient's data was recorded using a checklist which contained socio-demographic information and patient's diagnosis and RDW results from the SYSMEX 2000i hematological analyzer.

4.7.4. Sample collection and processing

As part of their clinical management, whole blood was collected into five ml EDTA vacutainer tubes. The collected samples were analyzed on Sysmex XT-2000i Hematology analyzer following standard operating procedure (SOP) To control the bias the outlier samples were run repeatedly.

4.7.5. Principle of Sysmex XT-2000i Hematology analyzer

The Sysmex XT-2000*i* Automated Hematology Analyzer is a 5-part differential analyzer which utilizes the power of fluorescent flowcytometry and hydrodynamic focusing technologies. Using a unique diode laser bench, Sysmex fluorescent flowcytometry provides the sensitivity needed for measuring and differentiating cell types in whole blood and body fluid samples. Fluorescent flow technology and hydrodynamic focusing enable the XT-2000*i* to consistently classify normal WBC, RBC and PLT populations form abnormal populations, thereby decreasing the number of manual interventions. XT-2000*i* technology provides clinically relevant and reportable parameters.

RBCs and platelets are counted using the direct current detection method with hydrodynamic focusing technology to minimize coincidence or recirculation. The intensity of the electronic pulse from each analyzed RBC is proportional to the cell volume. The HCT is directly determined based on the count and volume detection of each individual RBC.

The Sysmex sodium lauryl sulfate (SLS) method for hemoglobin analysis is a non-cyanide method. Hemoglobin is determined in a separate channel, minimizing interference from high leukocyte concentrations.The combination of side scatter (inner complexity of the cell), forward scatter (volume) and fluorescence of nucleic acid material determines the classification of each WBC.Fluorescent technology is also used to offer efficient and reproducible analysis of the reticulocyte count and maturation stages. The advanced technology allows an accurate count of reticulocyte and fluorescent platelets, even in extremely low concentrations and in samples with giant platelets or red cell fragments. The RDW is calculated as the coefficient of variation of the red cell volume and is expressed as a percentage (61).

4.8. Data Quality Control

The principal investigator was involved in every step of the process including disseminating questionnaires, analyzing patient's blood sample, analyzing healthy study subject's sample and running quality control on the SYSMEX 2000i hematological analyzer before running the case and control samples. Lab professionals involved in the data collection process were fully trained specific to this study. The objectives of the study were not disclosed to the data collectors in order to avoid bias. Advisors were supervising and guiding every process in order to make sure quality of the study is maintained in each step. Pre-testing and checking of all the questionnaires for errors, completeness and logical consistency at the end of each day, and giving prompt feedback at the spot during the data collection process were the methods employed to ensure the quality of data. Samples were only being run when daily controls lie within the acceptable limit. The laboratory SOP was strictly followed at all times.

4.9. Data Analysis and interpretation

The data was entered in to Excel spread sheet and imported for analysis to SPSS version 19 software (SPSS INC, Chicago, IL, USA). Patients were divided according to their RDW values and the type of non hematological disease they are diagnosed with. The continuous variables are presented as the means and standard deviations. Frequency was analyzed with 95 % confidence interval to assess the clinical utility of RDW in diagnosing the non-hematological disorders by clinicians. Chi-square was also calculated to show the statistical significant association between elevated RDW and of the non-hematological disorders. Paired t test was used to calculate the mean difference between patients with a heart, liver or kidney disease would have their RDW levels elevated comparing to the apparently healthy people. Percentages, tables and graphs were used for depiction of the data. P values less than 0.05 were considered statistically significant.

4.10. Operational Definition

Lab-marker: a parameter measured in a laboratory which can aid in the diagnosis and prognosis of diseases.

Clinicians: Medical professionals who work directly with patients.

Clinically Significant: Medically important

Clinical Utility: Medical usefulness in practice, observation, investigation, diagnosis or treatment.

Elevated RDW: Is red cell distribution width result above 14.5%.

Non-hematological diseases: Are diseases which are not blood related such as diseases of the heart, liver, kidney etc.

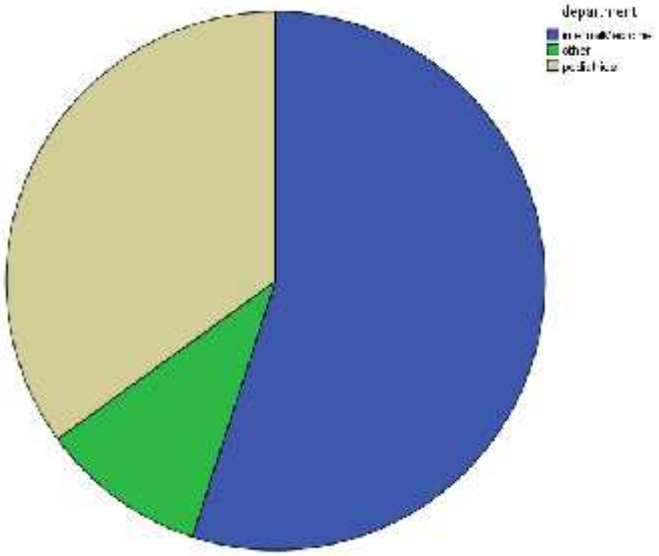
Red cell indices: are measurements that describe the size and oxygen-carrying protein (hemoglobin) content of red blood cells.

4.11. Ethical Considerations

The study was approved after it was reviewed by the research and ethical review committee of the department of medical laboratory science and department of internal medicine, School of Medicine at Tikur Anbessa Specialized Hospital College of Health Sciences, Addis Ababa, Ethiopia. Clinicians and patients were included after providing their consent. No additional blood samples were collected for the purpose of this study as patients for whom CBC was requested as part of their routine work up were included. For apparently healthy controls, the aim of this study was explained and 5 ml EDTA blood was collected based on their consent. Data confidentiality was maintained by password protecting electronic files and by locking hard copies throughout the study.

4.12. Dissemination of result

The Findings of this study will be submitted to Tikur Anbessa Specialized Hospital after the thesis defense at the department of medical laboratory sciences. So it can serve as a reference in the library. In addition, a copy of this material will be given to Ministry of Health, Addis Ababa Health Bureau, and respective hospitals to advocate for the utilization of the parameter. The result will also be disseminated through publication in peer reviewed local and international journals and through presenting it in relevant workshops and conferences.


department
other

5.1.2. Clinician's knowledge about utility of RDW in the investigation of cardiac, kidney and liver diseases

Knowledge that elevated RDW can aid in the investigation of heart, kidney and liver patients was assessed among clinicians. Overall, 51% of the clinicians responded “Yes” while the remaining 49% responded “No”. When data is disaggregated by specialty, 19/35 (54.3%) of the pediatricians, 24/55 (43.6%) of internists and 6/10 (60%)of the GPs and interns answered “No” while 31/55 (56.4%) and 16/35 (45.7%) of the internists and pediatricians, respectively, answered “Yes”(Table 1)

Table 1.Clinicians’ knowledge that elevated RDW can aid in the investigation of cardiac, kidney, liver disease at TASH from May- August, 2015.

Department/specialty	Knowledge about RDW		Total (n)
	Yes (n)	**No(n)**	
Pediatrics	16	19	35
Internal Medicine	31	24	55
GPs and Interns	4	6	10
Total	51	49	100

RDW=Red cell distribution width; GP=General practitioner; TASH=Tikur Anbessa Specialized Hospital

5.1.3. Clinical utility of RDW in the investigation and follow up of heart, kidney, liver and other non hematological diseases

Frequency was calculated to assess clinical utility of RDW in the investigation and follow up of heart, kidney, liver and other non hematological diseases at TASH from May-August 2015. Out of the 35 pediatricians, 2, 3& 9 of them use RDW always, frequently or sometimes respectively. The rest 21/35 (60%) rated that they rarely or never use the parameter in the investigation of non hematological diseases. Out of the 55 internists who participated in the study, 40 (72.7%)of the internists rated that they rarely or never use RDW, however, only 1 reported the frequent use of the parameter. The other 13(23.6%) rated that they sometimes use RDW. All of the 10 general practitioners and Interns rated that they sometimes or never use this parameter. From the total percentage, 68% of the doctors rated that they rarely or never use RDW in the investigation or follow up of the patients. (Figure 2)

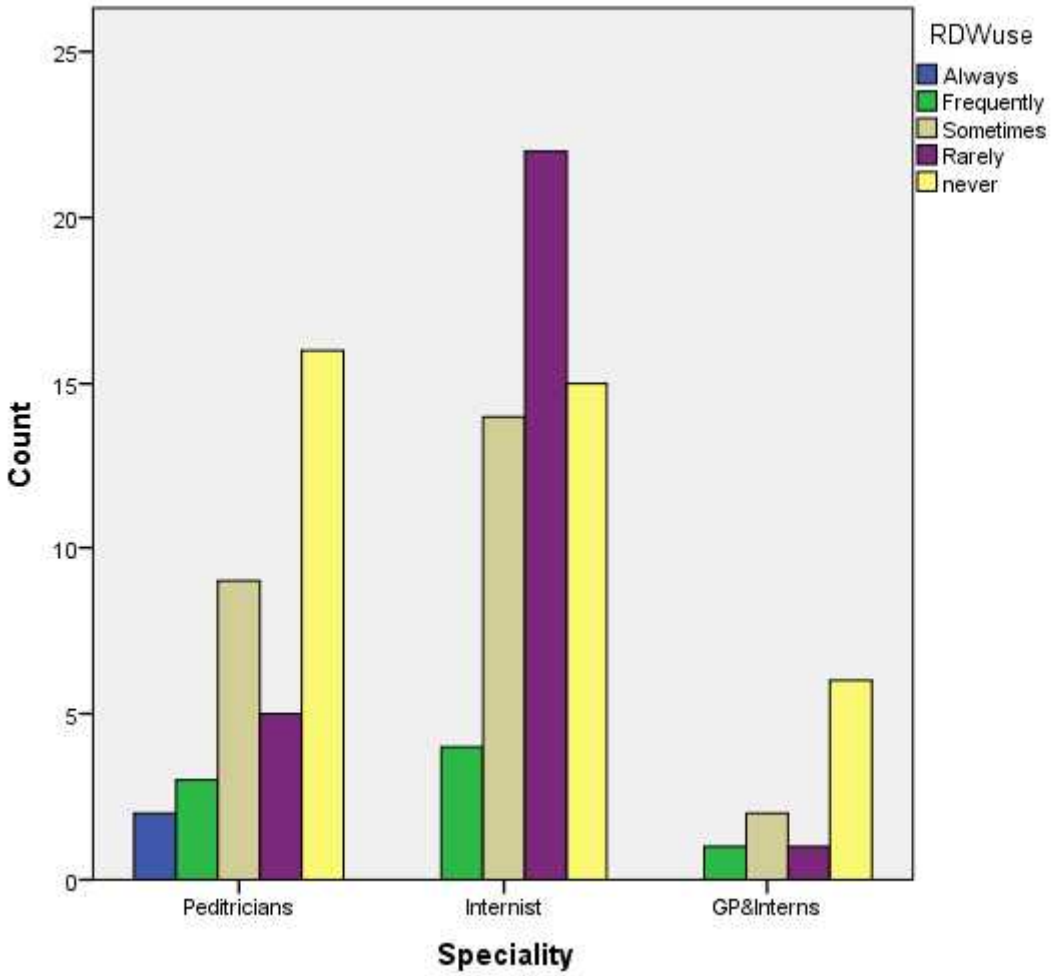

RDWuse
Always
Frequently
Sometimes
Rarely
never
Count
25
20
15
10
5
0
Peditricians
Internist
GP&Interns
Speciality

Table 2. Feedback of clinicians on clinical conditions RDW is utilized at TASH from May-August, 2015.

Department	Clinical conditions RDW is utilized				Total (n)
	Anemia	Non-hematological conditions	No response	Never use it	
Pediatrics	20	5	9	1	35
Internal Medicine	31	8	16	1	55
GPs and Interns	1	2	5	2	10
Total	52	15	30	4	100

RDW=Red cell distribution width; GP=General practitioner; TASH=Tikur Anbessa Specialized Hospital

5.1.5. Adequacy of clinical laboratory methods (CLM) course in medicine

Half (50%) of Clinicians feedback indicated that in the clinical laboratory methods course the introduction of RDW as a clinical significant parameter in the investigation and follow up of heart, kidney, liver and other non hematological diseases, was fair to poor, While 18% of the clinicians rated that it was excellent or very good. The remaining 32% rated good. (Table 3)

Table 3. Feedback of clinicians on adequacy of clinical laboratory methods (CLM) course in Medicine to introduce clinical significance of RDW at TASH from May- August, 2015.

Department	Adequacy of CLM course in medicine					Total
	Excellent	Very Good	Good	Fair	Poor	
Pediatrics	2	5	8	7	13	35
Internal Medicine	3	7	20	7	18	55
GPs and Interns	0	1	4	0	5	10
Total	5	13	32	14	36	100

RDW=Red cell distribution width; GP=General practitioner; TASH=Tikur Anbessa Specialized Hospital

5.1.6. Association between RDW use and year of experience

Pearson chi-square was utilized in order to establish association between specialist's year of experience and RDW use at TASH it was found that the association was not statistically significant ($p>0.05$).

Table 4. Association between RDW use and Clinician's year of experience at TASH from May- August, 2015.

Year of Experience	RDW Use					Total
	Always	Frequently	Sometimes	Rarely	Never	
0-7	2	7	20	26	33	88
8-15	0	0	2	1	1	4
16-23	0	1	3	1	1	6
24- 31	0	0	0	0	2	2
Total	2	8	25	27	36	100

	value	Confidence Interval (95%)		P value		
		upper	lower			
Pearson chi square	8.3	0.535	0.725	0.63		
Total	5	13	32	14	36	100

RDW=Red cell distribution width TASH=Tikur Anbessa Specialized Hospital

5.2. RDW values in the case and control groups

5.2.1. Distribution of RDW value for the case(heart, kidney and liver) and control (apparently healthy people) group.

The mean and range of RDW were calculated for both groups. Paired t test of RDW was also calculated. The Mean ±SD RDW value for cases was 15.2±3.37(Range= 12.1-31.1) which was significantly higher than the control groups. The corresponding RDW values for the control group were 13.3±0.79 (Range=11.9-15.8).Paired t test revealed a P value with 95% confidence interval of (CI= 1.31-3.75, $P<0.001$) (Figure 3).

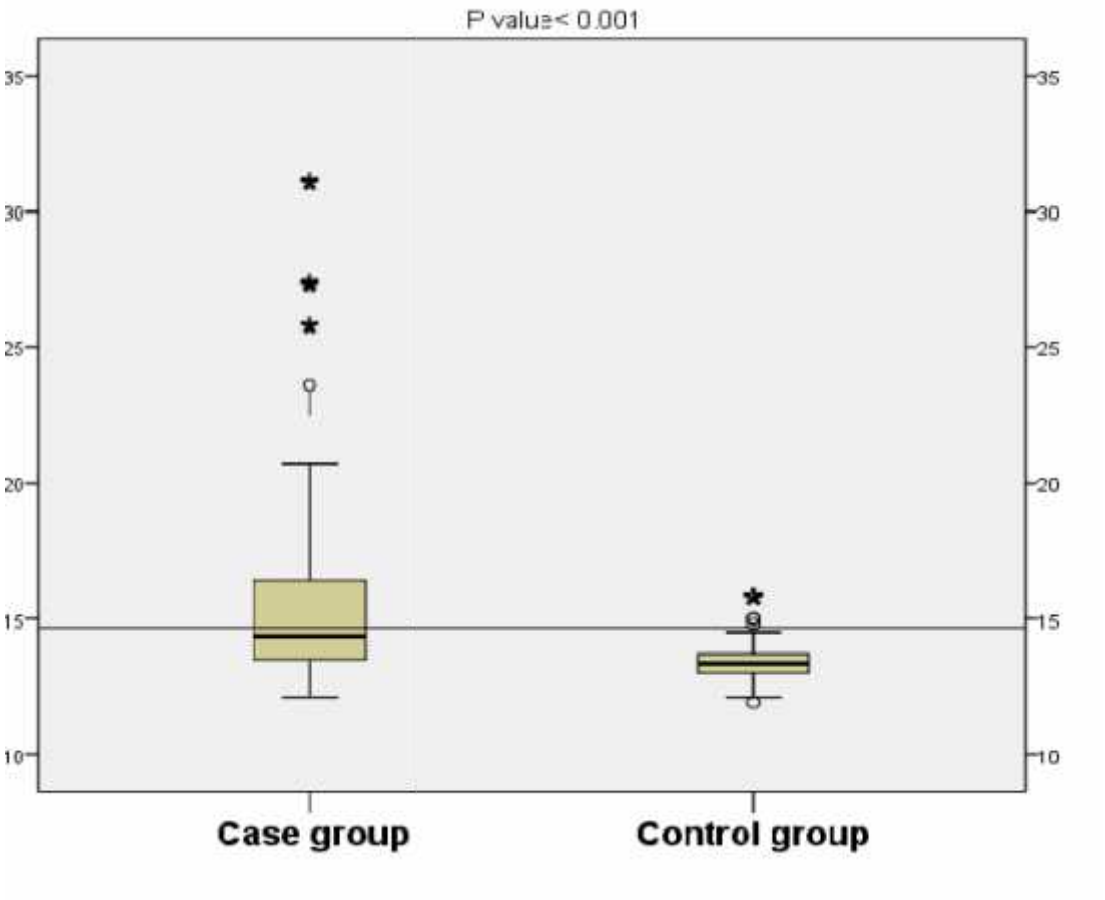


Figure 3. Whiskers and box plot of distribution of RDW value for the case (cardiac, kidney and liver patients) and control group (apparently healthy) at TASH from May-August, 2015.

5.2.2. Association between elevated RDW value and the disease type (cardiac, kidney& liver)

Elevated RDW value (>14.5) was observed in 40% of the cases and only 8% of the apparently healthy controls had elevated RDW values. Pearson chi-square test was employed to determine the association between the disease types and elevated RDW results and the association was found to be statistically significant (P<0.05) with 95% confidence interval (0.000-0.030). Out of the 40 heart patients, 20 (50%) of them had elevated RDW(RDW>14.5). From the total number of 32 kidney and 28 liver patients, 6 and 14 (50%) of them had elevated RDW respectively (RDW>14.5).(Table 4)

Table 5: Association between elevated RDW and disease types(hear, kidney & liver) at TASH from May- August, 2015.

Disease type	RDW result		Total	P value
	Normal(RDW=11.5-14.5)	Elevated (RDW> 14.5)		
Heart	20	20	40	0.01
Kidney	26	6	32	
Liver	14	14	28	
Total	60	40	100	

	Value	Confidence interval(95%)	
		Lower bound	Upper bound
Pearson Chi square	8.854	0.000	0.030

5.2.3. Association between Age, Sex and Elevated RDW in the case group (heart, kidney and liver patients) at TASH from May- August 2015.

Median for age in the case and control group was calculated to be 38 (Range=18-79) and 35 (Range= 22-70) respectively. Percentage of male and female patients in the case group were 53% and 47% respectively. In the control group, 46% were male and 54% were female. The association of age and elevated RDW in the case group was not found to statistically significant (P=0.967). Similarly, the association between sex and elevated RDW was not statistically significant (P=0.1).

6. Discussion

The study aimed at assessing the knowledge and clinical utility of RDW in the investigation of non hematological disorders at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. By using a self administered questionnaire. It had established that the clinical utilization of RDW in the investigation and follow up of heart, kidney and liver diseases was insufficient. Another research's findings supported the present study stating that RDW was the least frequently utilized parameter (5). In contrary, a study conducted in 2009 reported that clinicians utilize RDW in the investigation as well as follow up of cardiac patients, establishing that RDW is an important parameter which can aid as predictive parameter for the outcome of a disease and support clinician's decision in choosing treatment for the patients (4). Moreover, study conducted in 2015 by Xu also contradicts with our study reporting that clinicians are widely using RDW in the investigation inflammation and liver fibrosis caused by hepatitis B infection (56). In china, there was a research done by Huang *et al* which reported that clinicians utilized RDW as a predictive index of mortality rate for acute kidney patients which contradicted the findings of our study (22).

Knowledge that elevated RDW is an indicator of non hematological diseases is an ongoing research which is investigating not only the association between elevated RDW and heart, kidney, liver diseases but also other diseases including different malignancies. Clinicians who participated in our study stated that half of them had the knowledge yet failed to apply it. Half of the clinicians who participated in the study rated the introduction of RDW in clinical laboratory methods course for medicine students as fair to poor. A study conducted in Ethiopia by Birhaneselassie *et al* supported these results urging that there should be better curriculum which incorporates updated studies regarding the association of elevated RDW with the diseases other than the hematological ones (31).

RDW is commonly used to manage patients with anemia. More than half of the clinicians at TASH reported that RDW was only clinically utilized for the diagnosis and investigation of different kinds of anemia including IDA. Only less than a quarter of the clinicians reported that they use it in the investigation of non hematological diseases. Along with many text books and studies including a study conducted in 2015 by Liu *et al* agrees with our findings stating that RDW is widely utilized for the management of patients with anemia (62). Our study aimed to create awareness among clinicians that RDW is clinically significant in the investigation of not only anemia but also non hematological diseases.

Association between clinician's year of experience and RDW use was considered in the present study but the result was not statistically significant. Our result contradicts with a survey conducted in America by Sandhaus *et al* which found a statistically significant association between year of experience and RDW use ($P<0.05$). Clinicians who worked for less than 10 years used RDW a lot more than clinicians who worked for more than 10 years (5). This finding entail that RDW's clinical significance in the investigation of non hematological diseases is relatively new idea and still being exhaustively researched. Researchers and educators at TASH should be updating students concerning current findings.

This study, to the best of our knowledge, is the first of its kind in Ethiopia which tried to identify clinical utility of RDW by obtaining feedback from clinicians and tried to establish the clinical significance of RDW by conducting a case control study. There is a statistically significant mean difference between the RDW value in the case ($15.2\pm3.36\%$, $p<0.001$) and in the control group(13.39 ± 0.79). This shows that patients with heart, liver or kidney diseases had elevated RDW as oppose to apparently healthy people suggesting the need for introducing the parameter in the clinical management of such patients.

Normally, patients with chronic diseases such as heart, liver or kidney diseases are bound to develop anemia of chronic diseases as a result they will have increased RDW. Anemic patients were excluded from our study for such reasons and in attempt to prove that RDW can be an early independent marker in the investigation of these non hematological diseases. A case control study by Lou *et al*, found that there was a statistically significant mean difference between the case(chronic liver patients) ($16.376\pm2.43\%$, $P<0.001$) and apparently healthy people ($13.03\pm1.33\%$) which corresponded with our findings (16). Another study conducted by Oh *et al* found that patients with kidney diseases had a mean of 15.7 ± 2.3 with a range of 11.7-28.0 which is in line with our study (20) .

Association of elevated RDW and heart, kidney and liver diseases was found to be statistically significant with 95% confidence interval (CI: 0.000-0.030, $p=0.01$). Out of the 40 heart patients, half (50%) had elevated RDW(RDW> 14.5). A systematic analysis of cohort studies by Huang *et al* also documented similar findings with our study , in which patients with Heart failure had 1% RDW increase especially those with fatal outcomes (95% CI: 1.06–1.14, $P=0.01$) (49). Patient outcome was not studied in our study. However, it is important to have a better understanding of the association between elevated RDW and non hematological diseases.

Explanation why or how patients with heart diseases had elevated RDW without onset of anemia is that the elevation of RDW may describe an underlying inflammatory state which might lead to impaired erythrocyte maturation. In addition, inflammatory cytokines released due to heart disease may impact normal bone marrow function and iron metabolism (63). The scientific explanation behind elevated RDW in non hematological diseases was not investigated in our study. There was also a statistically significant association between elevated RDW and kidney patients (95% CI: 0.000-0.30, P=0.01). Out of the 32 kidney patients, 19% had elevated RDW (> 14.5). In another study conducted by Oh *et al*, they found that out of the total number of kidney patients enrolled in the study 67.5% of them had elevated RDW (≥14.6). The study went on to disclose that there was a statistically significant association between elevated RDW and fatality due to kidney diseases (RDW value= 16.0± 2.5, P< 0.01) (20). In our study, there was no follow up or investigation of clinical outcomes of patients with kidney diseases.

Regarding liver patients, it was found that out of the total number who participated in this study, half of them had elevated RDW level (> 14.5) with an established the association using Pearson chi square test (95% CI: 0.000-0.030, P<0.001). In consistence with this, Cengiz *et al* also found that elevated RDW (> 14.5) had a statistically significant association with liver diseases especially patients with severe fibrosis (95% CI: 1.129-2.711, P<0.01) (57). Similar findings were reported by Lou *et al* who found a statistically significant association with elevated RDW and chronic liver disease (P<0.001). The study further concluded that patients with higher RDW levels were at higher risk of fatal outcomes. Again patient follow up or clinical outcomes of patients with liver diseases were not performed during the course of our study (16).

The scientific cause behind elevation of RDW levels in liver or kidney patients has not been investigated in our study. Along with RDW levels, investigation of other non hematological parameters could have helped with the identification of the source behind increased RDW level in those patients. This is a potential limitation of our study.

A study conducted in 2009 reported that RDW was significantly associated with low cholesterol level indicating malnutrition and also there was a relationship with WBC count indicating inflammation. Inflammation and malnutrition might be associated with adverse clinical outcomes of seriously sick patients (64). A recent study by Tekce confirmed inflammation and malnutrition are associated with elevation of RDW in patients with kidney diseases who had worse clinical outcomes without anemia than patients without sign of inflammation or malnutrition (Mean= 18.5 ±2% versus Mean= 13.2±1.4%, P=0.004) (53).

Statistically significant association did not seem to exist between neither age and elevated RDW levels nor for sex and elevated RDW level (P=0.967, P=0.1 respectively). In line with our findings, a study conducted by Tekce reported that there was no statistically significant association between age and elevated RDW levels or sex and elevated RDW level (P= 0.463, P=0.822 respectively) (52). Although, Lou *et al* demonstrated that there was a statistically significant association between age and elevated RDW level (> 15) (P<0.003), the same study found no statistically significant association between sex and elevated RDW (P=0.77) (16).

Considering this study is the first of its kind, it tried to assess and identify the gap existing and create awareness as much as possible by presenting scientifically proved facts and findings. It's our belief that, our study will contribute to the improvement of the health care service by increasing awareness among clinicians. TASH being a center where several specialty and subspecialty level clinical services and trainings being offered, introducing this simple and easily available parameter in this hospital could help to easily cascade to other health facilities in the country. This research can be used as a start, initiating other researchers to investigate the gaps stated in our study and formulate a scientific answer towards the problem. Along with the three diseases investigated in our study, elevated RDW level has been reported to be associated with many diseases.

7. Strength and Limitation

7.1. Strength

- This research is the first one to be done in Ethiopia, best of our knowledge, providing basic awareness of RDW's clinical utility and establishing the association between elevated RDW and heart, kidney and liver diseases.
- This study provided evidence for educators, scientists and Doctors in Ethiopia to teach, conduct further research and clinically utilize RDW.
- This study puts us one step further in utilizing a simple but neglected marker to the clinical management of non hematological diseases, thus, improving the health care delivery.

7.2. Limitation

- Follow up of the patients, documentation of their progress and outcome should have been performed.
- Detection of inflammatory cytokines was not performed in the participants to investigate the scientific explanation behind elevated RDW without onset of anemia.

8. Conclusion and Recommendation

8.1. Conclusion

- RDW's clinical utility at TASH in the investigation or follow up of patients with non hematological diseases by clinicians was insufficient indicating that awareness should be created. Half of the clinicians had the knowledge that elevated RDW could be an indication of non hematological diseases yet failed to utilize it. Reason behind it is yet be identified but the habit of utilizing RDW in the investigation of diseases other than anemia should be urged and encouraged.
- The adequacy of CLM course in medicine was rated fair to poor by most clinicians, proving that the course needs to be dynamic by incorporating different study findings which will support the education to be all rounded and updated.
- There was no statistical significant association between year of experience and RDW use which shows that RDW is a newly researched parameter in the investigation of non hematological diseases and the awareness has not been yet created in Ethiopia.
- There was a statistically significant mean difference between the case and control group . This establishes RDW can assist in the investigation of non hematological diseases.
- There was a statistically significant association between elevated RDW and non hematological diseases confirming that patients suffering from heart, kidney or liver diseases had elevated RDW independent of anemia establishing that RDW is a clinically significant marker which should be used more often.

8.2. Recommendation

It is my general recommendation that clinical laboratory methods course should be improved and should incorporate updated research findings regarding association of RDW with many diseases. Clinicians should pay attention to RDW results as well as the other parameter they usually notice while investigating patients with heart, kidney and liver diseases. It is recommended that RDW should be clinically utilized frequently in the investigation of variety of hematological as well as non hematological diseases as the rest of the world does. Longitudinal research is recommended to be carried out in order to figure out the relationship between elevated RDW and the outcome of non hematological diseases. The scientific explanation behind elevated RDW in non hematological diseases has not been investigated in our study encouraging to be investigated in future studies.

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Sampler (Auto) Mode

Standard precautions should be followed when handling specimens and performing all laboratory testing.

1mL of sample required.

Place specimens in a rack with barcodes facing the front of the rack. Ensure that labels are securely adhered to tube with no loose edges.

Load up to 5 racks at one time (50 samples). A new rack may be added to the right rack pool at any time.

On the computer, click on the “Sampler” icon or press [F3] on the keyboard. The “Sample Number” dialog box displays.

Click [SAMPLER START]and [OK].

The specimen will be automatically mixed the sample 10 times, aspirates, and analyzes the sample according tothe tests ordered for specified barcode. Results will print if specimen meets criteria that require further action by the technologist (ie. smear reviews, manual differentials, repeat of critical results).

Note: If Barcodes are not used, the sample number will increment by 1 as each sample is analyzed. The discrete test to be performed must be selected in the Sampler dialog box.

Manual Mode

85 uL of sample required (short drawor pediatric capillary collection).

Click the “Manual” icon or press [F2]on the keyboard.

Enter the specimen number using the keyboard or the handheld barcode wand.

Discrete tests for manual mode are defaulted to C/D/R (CBC/Diff/Retic) unless changed by the operator.

Click [OK].

Mix the patient sample. Uncap the tube.

Place sample under the aspiration pipette so that the tip of the pipette is at the bottom of the sample tube.

After sample aspiration a part of the whole blood sample is diluted in 1:50 with lysing reagent stromatolyse4DL and then stromatolyer 4ds dye is added.

After a pre defined response time the stained sample is introduced into the detector, where forward light scatter and side fluorescent emission are measured. From this four leucocyte populations are computed: neut count (neu #), lymph count (lymp#), mono count (mono#) and eos count (eos#) as well as neutr percentage (neu %), lymp %, mono%, eos%.

Reagent of sysmex XT-2000i

1,CELLPACK – diluents for use in hematology analyzers.

It is ready to use diluents for impedance and photoelectrical analysis of whole blood.

Ingredients: sodium chloride, boric acid, sodium tetra borate, EDTA-2K

2, STROMATOLYSER – FB

Is a ready to use lysing reagent to analyze to leucocytes and the basophilic granulocytes of a whole blood sample by resistance measurement and photometric measurement.

Ingredients: non ionic surfactant, organic quaternary ammonium salt

3, STROMATOLYSER -4DL

It is a ready to use diluents for analyzing blood by resistance and photometric measurement.

Ingredients: non ionic surfactant, organic quaternary ammonium salt.

4, STROMATOLYSER-4DS

It stains the leucocytes in diluted and lyses blood samples. Ii serves for the determination of 4 part differential count (lym, mono, eos, neu+ baso) with selected sysmex hematology analyzers.

Ingredients: Polymethine dye, methanol, ethylene glycol.

5, SULFOLYSER

It is ready to use diluents, for analyzing blood by photoelectrical analysis. It is a cyanide free reagent used for the determination of hb. lyses the erythrocyte and acts upon globin of hemoglobin to form a stable hemochrome. SULFOLYSER is intended for use on all sysmex automated hematology analyzers excluding model of CC and M series

Ingredients: sodium lauryl phosphate

6. RET SEARCH (II) (diluents)

RET SEARCH (II) (dye solution)

RET SEARCH (II) is intended to diluents the sample while simultinously staining the reticulocyte to assay the reticulocyte concentration in blood with sysmex hematology analyzer.

RET SEARCH (II) is a pre packaged reagent kit consisting of RET SEARCH (II) diluents buffer and RET SEARCH (II) dye. Both reagents are only used by the XT 2000i.

Methodology: RET SEARCH (II)is a ready to use diluents with a matching dye for analysis of whole blood by resistance measurement and photometric measurement.

Ingredients: RET SEARCH (II) (diluents): tricine buffer,

RET SEARCH (II) (dye solution): polymethinedye , methanol, ethylene glycol.

7, CELLCLEAN

Is a strong alkaline detergent to remove lysing reagents, cellular residuals and blood proteins remaining in the hydraulics osfsysmexanalyzer.

Is a detergent to clean the instrument, to remove residual and blood proteins from the hydraulic systems, transducer, sample rotor valve, whole blood aspiration tube and hb flow cell.

Ingredients: sodium hypochlorite

Annex II*:* Subject Information Sheet (English) For Clinicians

Questionnaire for data collection on the survey of the clinical utility of RDW in diagnosing non-hematological disorders from May-August 2015 Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: A Case Control Study.

Greetings!

My name is Melatwork Tibebu, a Master of Clinical Laboratory Science student at Addis Ababa University, College of Health Sciences, and Department of Medical Laboratory Science. The study will find out the clinical utility of RDW in diagnosing non-hematological disorders by clinicians. The survey is undertaken by a Questionnaire which is a single page, double sided paper containing clear questions which are tailored to the objective of the research. It will not take more than 5 minutes to fill in the Questionnaire. In addition from the questionnaire which is going to be filled by clinicians, RDW results from blood samples of cardiac, liver and kidney patients as well as apparently healthy patients is going to be utilized to establish the association between RDW and the diseases. The data from the Questionnaire and the RDW results will be utilized only for the research purpose. The Questionnaire filled and the RDW results would not be identified by person and the confidentiality would be kept. Once the data is utilized for the research purpose the collected information and the Questionnaire would be destroyed. You are kindly requested to fill in the Questionnaire to provide supportive data for the above mentioned rationale. You will not have any obligation to fill in the questionnaire if you are not willing to do so for any of your reasons.

For any information you can contact: Ms. Melatwork Tibebu

Tel 0931566437,

E-mail: melatworktibeb@yahoo.com

Institutional Review Board (IRB):

Tel: 011- 896 1396

E-mail: aaumfirb@yahoo.com Fax +251-1-1-513099

Annex III: Subject Information Sheet (Amharic) For Patients

ይህ መጠይቅ በአዲስ አበባ ከተማ ሆስፒታሎች ውስጥ ሀኪሞች ምን ያህል የቀይ ደም ሴሎች ላይ ከሚሰሩ የተወሰኑ የላባራቶሪ ጥናቶች ለልብ፣ ለኩላሊትና ለጉበት በሽተኛ በሚጠቅም መልኩ እንደሚገለገሉበት የሚያጠና ነው።

የቃል ስምምንት

እንደምኖት የኔ ስም ሜላትወርቅ ጥበቡ ይባላል።

በአዲስ አበባ ዩንቨርሲቲ ህክምና ላብራቶሪ የክሊ ኒካል ላብራቶሪ ሳይንስ የማስተርስ ተማሪ ነኝ።

ይህ ጥናት የቀይ ደም ሴሎች ላይ የሚሰሩ የተወሰኑ የምርመራ አይነቶች በምንያህል ደረጃ የጥቁር አንበሳ ሆስፒታል ሀኪሞች ለልስ፣ ኩላሊት ጉበት በሽተኛ ህክምና ድጋፍ ላይ እንደሚያውሉ የሚያጠና ነው በተጨማሪም ሀኪሞቹ እነዚህን ምርመራ አይነቶች እንዳይጠቀሙ የሚያደርጉአቸው ችገሮች ካሉም ለመ ሌትና መፍትኤ ለማቅረብ ይሞክራል።

ጥናቱ በመጠይቁ በተዘጋጁ ፎርም የሚካሄድ ሲሆን መጠይቁ ከ5 ደቂቃ በላይ የማይፈጅ ነው።

መጠይቁም የሚውለው ለተጠቀሰው ናት አላማ ብቻ ሲሆን ለሚስትራዊነቱም የተጠበቀ ነው።

መጠይቁም ለጥናቱ ግልጋሎት ከላይ ከዋለ በኋላ ይቃጠላል፡ በዚህ ጥናት ላይ መሳተፍ በርሶ ፍቃደኝነት ላይ የተመሰረተ ነው። እርሶ በተስማት ማናቸውም ምክንያት መጠይቁን ላለመላት ከፈለገፉ መብትበእጀ ነው።

ሜላትወርቅ ጥበቡ

ይህ ጥናት በተመለከተ ወይም ከዚህ ጥናት ጋር በተዛመደ መልኩ ስለሚያጋጥሙ ድንገተኛ አደጋ ችግሮች ወይም ጥያቄ ካለት በሚከተለው አድራሻ ይጠቀሙ።

ሜላትወርቅ ጥበቡ

ሞባይል 0931566437፣ ኢሜል፡

ለተጨማሪ መረጃች የአዲስ አበባ ዩንቨርሲቲ ህክምና ፋኩልቲ ኢንስቲትዩሽናል ሪቪው ቦርድ ይጠይቁ።

ስ.ቁ፡-251-11-5-53-87-34 ፋክስ ፡-251-11-5-51-30-99 ኢ-ሜል፡ aaumfirb@yahoo.com

Annex IV: Consent Form (English)

I have read the information sheet above and clearly understood the purpose and anticipated benefit of the research. I hereby need to assure with my signature below that I, without any coercion or forceful act by the research team, have decided to voluntarily participate in the study to contribute my part in the effort being made for the understanding of the clinical utility of RDW in diagnosing non-hematological disorders by clinicians at Tikur Anbessa Specialized Hospital.

Unique ID No._____ Signature _____ Date_____

Interviewer's name _____Signature_____

Date of interview_____Time started_____Time finished_____

Supervisor's Name_____ Signature_____

I thank you for your cooperation

Please direct any questions or problems you may encounter during this study to:

Melatwork Tibebu; Department of Medical Laboratory Sciences - Addis Ababa University. Mobile 0931566437, melatworktibebu@yahoo.com.

For additional information, please contact Addis Ababa University Medical Faculty Institutional Review Board (IRB) office at:

Tel: +251-11-896 1396

Fax 251-11-5-51-1-51-30-99,

P O Box 9086, Addis Ababa, Ethiopia.

E-mail: aaumfirb@yahoo.com

Annex V: Consent Form (Amharic)

ከላይ የተጻፈውን የመረጃ ሀሳብ አንብቤ ፣የጥናቱን አላማበግልጽ የተረድቻለሁ;፡ በዚህም መሠረት ለጥናት ቡድኑ አባላት ያለምንም ትእኖ በሙሉ ፈቃደኝነት በዚሁ ጥናት በመሳተፍ በደም ናሙና ላይ ለሚደረጉ የላብራቶሪ ምርመራ አገልግሎት መሻሻል በማድደርገው ጥረት ውስጥ የበኩሌን አስተዋጸ ለማበርከት መወሰኔን በፊርማዮ አረጋግጣለሁ፡፡

የተጠያቂው መለያ ቁጥር---------- ፊርማ----------ቀን----------

የመረጃ ሰብሳቢ ስም ---------- ፊርማ----------ቀን----------

መረጃ የተሰበሰበለት ስም ---------- የተጀመረበት ሰዓት----------ቀን----------

የተቆጣጣሪ ስም ----------ፊርማ ----------ቀን ----------

ይህን ጥናት በተመለከተ ወይም ከዚህ ጥናት ጋር በተዛመደ መልኩ ለሚያጋጥሙን ችግሮች ወይም ጥያቄ ካሎት በሚከተለው አድራሻ ይጠቀሙ፡፡

ሜላትወርቅ ጥበቡ ሞባይል 0931566437፣ **ኢሜል**፣ melatworktibebu@yahoo.com

ለተጨማሪ መረጃች የአዲስ አበባ ዩንቨርሲቲ ህክምና ፋኩልቲ ኢንስቲትዩሽናል ሪቪው ቦርድ ይጠይቁ፡፡

ስ.ቁ፡-251-11-5-53-87-34

ፋክስ ፡-251-11-5-51-30-99

ኢ-ሜል፡ aaumfirb@yahoo.com

Annex VI: Subject Information Sheet (for healthy participants, English)

Title of the Research Project: The Clinical Utility of RDW in Diagnosing Non-Hematological Disorders from May-August 2015 at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: A Case Control Study.

Name of Investigator: Melatwork Tibebu (BSc)

Name of the Organization: Addis Ababa University, College of Health Science, Department of Clinical Laboratory Science.

Greetings!

You are invited to participate in a study to be conducted by MSC student at Addis Ababa University, College of health sciences, School of Allied Health Science, Department of Medical Laboratory Sciences. It is aimed at determining the Clinical Utility of RDW in Diagnosing Non-Hematological Disorders at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

This study aims to establish RDW as a lab marker for non hematological disorders such as heart, liver and kidney diseases by comparing it with healthy patient's RDW so that RDW will be recognized as a lab marker and more frequently utilized for diagnosis and prognosis of patients by clinicians in Ethiopia. Please read the following statements and ask any unclear points before you agree to participate.

Participation in the study is voluntary. If you are not willing to participate in the study or if you want to withdraw even after deciding to participate, there will be no consequences. If you decide to participate, you have to sign the consent form and you can get a copy of this information sheet.

What is expected from you as a participant of the study?

As a participant of this study you are expected to give 3-4 ml blood. You need to know that the results might be discussed with appropriate individuals out of this hospital. But your name, address and phone number will not be disclosed to anyone and to be more precise, identification code will be used in such conditions.

How long participation will take you?

You will spend 5-10 minutes until the specimen is collected and the consent is signed.

What are the risks of participating in this study?

There are no anticipated risks to your participation except minor discomfort during venipuncture because well experienced professionals will collect blood samples.

How the information is to be kept confidential?

All information that you give and the results from your specimen will be used for this study only. Only limited number of professionals will have access to the information. All the information will be encoded in a computer and will be password protected.

What are the benefits from participation?

Since this study is MSc student research, there will not be payment for participants. But your participation is vital for establishing RDW as a lab marker for non hematological disorders such as heart, liver and kidney diseases by comparing it with healthy patient's RDW so that RDW will be recognized as a lab marker and more frequently utilized for diagnosis and prognosis of patients by clinicians in Ethiopia.

What are your rights as a participant of this study?

You can ask any question questions for further explanation. The principal investigator and the data collectors are responsible to clear any doubt you may have during participation. You have the right to get the results of the analysis.

Please forward any question or problems you may encounter during this study to Melatwork Tibebu, Department of medical laboratory science School of Allied health sciences

College of health sciences

Addis Ababa University

Mob: +251-931- 56 64 37

Email: melatworktibebu@yahoo.com

Annex VII- Subject information sheet (Amharic)

የአዲስ አበባ ዩንቨርሲቲየጤና ሣይንስና ኮሌጅ የአላይድ ጤና ሣንስ ት/ቤት ይሕክምና ላቦራቶሪ ሣይንስ ለማጥናት ታስቦ ለተሳታፎዎች የተዘጋጀ መረጃ ሲሆን እርሶም በአዲስ አበባ ዩንቨርሲቲ ፡ ጤና ሳይንስ ኮለሌጅ የህክምና ላቦራቶረ ሳይንስ የማስተርስ ድግ ሪ ተማሪ የመመረቂያ ጠናት ላይ እንዲሳተፉ የጋብዘዋል፡፡ እባክዎ በዚህ ጥናት ለመሳተፍ ከመስመማትዎ በፊት ከዚህ ቀጥሎ የሚገኘውን ምንባብ በጥሞነ ያንብቡና ግልጹ ያልሆነውን/ኑትን ማንኛውም ሃሳብ ይጠይቁ፡፡

መግቢያ

እረስዎ በዚህ ጥናት ላይ የሞኖሮት ተሳትፎ ሙሉ በሙሉ በበጎ ፈቃደኝነት ላይ የተመሰረተ ነው፡፡ በዚህ ጥናት ውስጥ ላለመሳተፍ ወይም ለመሳተፍ ከተወሰኑ በኋላ ለማቋረጥ የሚወስኑ ቢሆንም እንኩዋ በዚህ ሆስፒታል የሚሰጠው ማንኛውም አገልግሎት አይቋረትም፡፡ በጥናቱ ለመሳተፍ የሚስማሙ ከሆነ የስምምነት ቅጹ ላይ በጹሁፍ ወይም በጣት ፊርማ ማስቀመጥ ይተበ ቅዎታል፡፡ ከፈለጉ ይህንን መረጃ አንድ ቅ ጅ ለራስዎ ሊያስቀሩ ይችላሉ፡፡

የጥናቱ ተሳታፊ በመሆኖ የሚጠበቅቦት ምንድነው

በዚህ ጥናት ለመሳተፍ የሚስማሙ ከሆነ የደም ናሙና ለመስጠት መስማመት ይጠበቅብዎታል፡፡ይሁን እንጅ ይህ አይነቱ መረጃ የርስዎን ማንነት የሚገል ጡ መረጃዎችን ማለትም ስም፣ አድራሻና ጠየስልክ ቁጥር የመሳሰ ሉትን መረጃ ዎችን አይጨምርም፡፡ ይልቁንም ለዚህ አገልግሎት ብቻ የሚውልና ለማወቅ የሚያስችል መለያ ቁጥር ላይ እንዲውል ይደረጋል፡፡ በተጨማሪም ስለርስዎ አጠቃላይ የጤና ሁኔታ ለሚቀርቡ አንዳንድ ተጨማሪ ጥያቄዎች መልስ መስጠት ይጠበቅብዎታል፡፡

በዚህ ጥናት መሳተፍ ምን ያህል ጊዜ ይፈጃል?

የተዘጋጀውን መጠይቅ ለመመላት፣ የስምምነት ቅጽ ላይ ለመፈረምና ናሙና ለመስጠት ከ20-35 ደቂቃ ያስፈልጋል፡፡

በዚህ ጥናት መሳተፍ የሚያስከትላቸው ችግሮች ምንድን ናቸው?

ናሙና በሚሰበስብበት ወቅት አይነት የከፋ ችግር አያጋጥምዎትም ምክንያቱም ናሙናው የሚወስደው ልምድ ባላቸው የጤና ባለሙያዎች በመሆኑ ነው፡፡

የእኔ የህክምና መረጃ በሚስጥር ተጠብቆ መቆየት የሚችለው እንዴት ነው

የሰጡት ማንኛውም መረጃና ከተወሰነው ናሙና ላይ የተገኘው የላብራቶሪ ውጤት የሚውለው ለጥረቱ አላማ ብቻ ነው፡፡ ይህንን ማ ህደር ሊያገኙ የሚችሉት የተወሰኑ የጥናትቱ ተባባሪ

ሰራተኞች ብቻ ናቸው፡፡ ከዚህም በላይ ስለስርሶ ያለውን ምናኛውም መረጃ የተለየ የይለፍ ቃል ባለው የኮምፒረተር የመረጃ ማህደር ውስጥ እንዲቀመጥ ይደረጋል፡፡

ይህ ጥናት የማስተርስ ዲግሪ መመረቂያ ጽሁፍ እንደቸመሆኑ መጠን ለተሳታፊዎች ገንዘብ አይሰጥም፡፡ ሆኖም ከጥናቱ የሚገኘው መረጃ ህሙማንን ህክምና ለማሻሻል አስተዋጾዎ ያደርጋል፡፡

የዚህ ጥናት ተሳታፊ መብቱ ምንድን ነው?

ከዚህም በተጨማሪ ጥናቱ በተመለከተ ማንኛውንም አይነት ጥያቄ የመጠየቅና ገለጻ የማግኘት መብት አለዎት፡፡ የላብራቶሪ ምርመራ ውጤቱንም በነጻሽ ማግኘት ይቻላሉ፡፡

ጥያቄ ካለኝ ወይም ችግር ቢያጋጥመኝ ምን ማድረግ ይገባል

ይህን ጥናት በተመለከተ ወይም ከዚህ ጥናት ጋር በተዛመደ መልኩ ስለሚያጋጥሙ ድንገተኛ አደጋዎች ወይም ጥያቄ ካለዎት በሚመለከተው አድራሻ ይጠ ቀሙ

ሜላትወርቅ ጥበቡ

የህክምና ላባራቶሪ ሳይንስ ት/ቤት

የጤና ሳይንስ ኮሌጅ

አዲስ አበባ ዩንቨርሲቲ

ሞባይል፡-251 931-56-64-37

የመረጃ ሰብሳቢ ስም ---------- ፊርማ----------

ቀን ----------

Annex VIII- Consent Form (English)

Code number----------

Name of the participant----------

I have been informed about the study which is aimed at determining the Clinical Utility of RDW in Diagnosing Non-Hematological Disorders and the Association between Elevated RDW and non-hematological disorders such as Heart, kidney and Liver diseases at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

The aims of the study and possible risks were explained to me as well.

I am also informed that all the information contained within the questionnaire is to be kept confidential. Moreover I have been well informed of my right to keep hold of information, decline to cooperate and make withdrawal from the study.

It is therefore with full understanding of the situation that I gave the informed consent voluntarily to the researcher to use my blood sample for the investigation. In addition, I have had the opportunity to ask questions about it and received clarification to my satisfaction. I have also been informed that the benefit of participation is to get the results of analysis from my sample measured for free via the counselor nurse.

Participant's signature /finger print ----------

Name of Data collectors ---------- signature---------- Date----------

Please direct any questions or problems you may encounter during this study to:

Melatwork Tibebu

Department of medical laboratory science

School of Allied health science

College of health sciences

Addis Ababa University

Mob: +251-931-56- 64-37

Email: melatworktibebu@yahoo.com

For additional information, please contact Addis Ababa University, College of Health Science institutional review board (IRB) office at:

Tell. +251-11-8-96-13-96

Fax +251-11-5-51-1-51-30-99

P.O. Box 9086, Addis Ababa, Ethiopia

Email: aau.mf.irb@yahoo.com

Annex-IX - Consent Form (Amharic)

የተሳታፊዎች ስምምነት ማረጋገጫ ቅጽ

የሚስጥር ቁጥር ----------

የተ ሳታፊው ስመ ----------

እኔ ስሜ ከላይ የተጠቀሰው ቦታዎች እንደ ልብ፣ ኩላሊት እና ጉበት ጋር ያለውን ግኑኝነት ላይ ስለሚደረገው ጥናት በቂ ገለጻ ተደርጎልኛል። ለትናቱም ከእኔ የተወሰደ የደምና ናሙና እንደሚያስፈልግ ተገልጾልኛል። የጥናቱንም አላማ ዎች በሚገባ ተረድቻለሁ።በመጠይቁ ላይ የገለጽኳቸው መረጃዎች በሙሉ በሚስጥር የተጠበቁ እንደሚሆኑ ተነግሮ ኛል። በትናቱ ላይ ያለመሳተፍና ማንኛውንም መረጃ ያለመስጠት እንዲሁም በማንኛውም ጊዘከጥናቱ ራሴን የግለል መብቴ የተጠበቀ እንደሆነ ተገልጾልኛል።

ስለዚህ ለዚህ ጥናት መረጃና ስምምነት ቃሌን የሰጠሁት በአጠቃላይ ሁኔታውን በመረዳትና በፍጽም ፍቃደኝነት ነው። የምሰጠውም ናሙና ለምርምር ብቻ እንደሚውልም ተረድቻለው። በተጨማሪም ጥያቄ ለመየየቅ ተፈቅዶልኝም ለማወቅ የፈለኩትን ያህል ማብራሪያ አግኝቻለሁ። የዚህ ጥናት ተሳታፊ በመሆኔ የሚገኘው ጥቅም የሁሉንም ምርመራ ውጤት በነጻ በማግኘት እነደሆነ ተረድቻለሁ።

የተሳታፊው ፊርማ/የጣት አሻራ----------

የምስክር	**ሙሉ ስም**	**ፊርማ**
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(የስምምነት ቅጽን ማንበብ ለማይችሉ ተሳታፊዎች)

የተሳታፊዎች ስምምነት ማረጋገጫ ቅጽ

የሚስጥር ቁጥር ----------

የተ ሳታፊው ስመ ----------

እኔ ስሜ ከላይ የተጠቀሰው ቦታዎች እንደ ልብ፣ ኩላሊት እና ጉበት ጋር ያለውን ግኑኝነት ላይ ስለሚደረገው ጥናት በቂ ገለጻ ተደርጎልኛል፡፡ ለትናቱም ከእኔ የተወሰደ የደምና ናሙና እንደሚያስፈልግ ተገልጾልኛል፡፡ የጥናቱንም አላማ ዎች በሚገባ ተረድቻለሁ፡፡በመጠይቁ ላይ የገለጽኳቸው መረጃዎች በሙሉ በሚስጥር የተጠበቁ እንደሚሆኑ ተነግሮ ኛል፡፡ በትናቱ ላይ ያለመሳተፍና ማንኛውንም መረጃ ያለመስጠት እንዲሁም በማንኛውም ጊዘከጥናቱ ራሴን የግለል መብቴ የተጠበቀ እንደሆነ ተገልጾልኛል፡፡

ስለዚህ ለዚህ ጥናት መረጃና ስምምነት ቃሌን የሰጠሁት በአጠቃላይ ሁኔታውን በመረዳትና በፍጽም ፍቃደኝነት ነው፡፡ የምሰጠውም ናሙና ለምርምር ብቻ እንደሚውልም ተረድቻለው፡፡ በተጨማሪም ጥያቄ ለመየየቅ ተፈቅዶልኝም ለማወቅ የፈለኩትን ያህል ማብራሪያ አግኝቻለሁ፡፡ የዚህ ጥናት ተሳታፊ በመሆኔ የሚገኘው ጥቅም የሁሉንም ምርመራ ውጤት በነጻ በማግኘት እነደሆነ ተረድቻለሁ፡፡

የተሳታፊው ፊርማ/የጣት አሻራ----------

የምስክር	**ሙሉ ስም**	**ፊርማ**
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	----------	----------

(የስምምነት ቅጽን ማንበብ ለማይችሉ ተሳታፊዎች)

Annex X-Questionnaire

1. Please, identify if you are:

A. Health Officer

B. General Practitioner

C. Specialist

D. Resident (Specify speciality)

E. Other (sepecify)

2. If you are a specialist, please indicate which area of specialty you belong to:

A. Pediatrics

B. Internal Medicine

C. Surgery

D. Obs-Gyn

E. Other (Please indicate) ----------

3. Year of experience in Clinical practice:_____

4. How often do you use RDW in investigation of medical conditions which are non-hematological?

A. Always

B. Frequently

C. Sometimes

D. Rarely

E. Never

5. How often do you use the RDW in investigation of patients who are suffering from cardiac diseases?

a. Always

b. Frequently

c. Sometimes

d. Rarely

e. Never

6.How often do you use the RDW in investigation of patients who are suffering from Kidney diseases?

a. Always

b. Frequently

c. Sometimes

d. Rarely

e. Never

7. How often do you use RDW in investigation of patients who are suffering from liver diseases?

a. Always

b. Frequently

c. Sometimes

d. Rarely

e. Never

8. Do you know if elevated RDW is an indication of diseases such as heart, kidney and liver diseases?

a. Yes

b. No

9. How often do you use RDW results in the follow up of those patients?

a. Always

b. Frequently

c. Sometimes

d. Rarely

e. Never

10. List conditions in which you use RDW for patient management _____

_____

_____

11. How do you rate the adequacy of Clinical Laboratory Methods course in Medicine, to introduce RDW and its clinical significance satisfactorily to medical students?

a. Excellent

b. Very good

c. Good

d. Fair

e. Poor

THANK YOU VERY MUCH FOR YOUR HELP

Annex XI: Checklist

Patient ID	Age	Sex	Diagnosis	RDW result

Annex XII: Declaration

I, the undersigned, declare that this MSc thesis is my original work, has not been presented for a degree in Addis Ababa University or any other universities. I also declare that all sources of materials used for the thesis have been duly acknowledged.

Name of the candidate Melatwork Tibebu (BSc)

Signature_____

Place: Addis Ababa University School of Medical Laboratory Sciences, Ethiopia

Date of submission_____/_____/_____

This proposal has been submitted with my approval as university advisor.

Name of advisor: Dr. Aster Tsegaye (MSc, PhD)

Signature _____

Date of submission_____/_____/_____

This proposal has been submitted with my approval as university advisor.

Name of advisor:Melaku Tamene(BSC, Msc, PhD candidate)

Signature _____

Date of submission_____/_____/_____

This proposal has been submitted with my approval as university advisor.

Name of advisor: Dr. Amha G/medhin (MD, Hematologist)

Signature _____

Date of submission_____/_____/_____