ADDIS ABABA UNIVERSITY
COLLEGE OF HEALTH SCIENCES
SCHOOL OF MEDICINE
DEPARTMENT OF INTERNAL MEDICINE

Atherosclerotic Cardiovascular Risk Assessment and associated factors among patients with Rheumatoid Arthritis at Tikur Anbessa Specialized Hospital Rheumatology referral clinic: Cross sectional study design

Principal Investigator: Yemisrach Kifle, Third Year Internal Medicine Resident

A Thesis to be Submitted to Addis Ababa University, College of Health Sciences, Department of Internal Medicine in Partial Fulfillment of the Requirements for Post Graduate/Residency Program in Internal Medicine

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Abbreviations and Acronyms

AAU	Addis Ababa University
ACCP	Anti-Cyclic Citrullinated Peptide
AHA/ACC	American Heart Association/American College of Cardiology
ASCVDs/CVD	Atherosclerotic Cardiovascular Diseases/Cardiovascular Diseases
CAD	Coronary Artery Disease
CDAI	Clinical Disease Activity Index
CRP	C-reactive protein
DAS-28	Disease Activity Score (28 Joints)
DMARDs	Disease Modifying Anti Rheumatic Drugs
EULAR	European Alliance of Associations for Rheumatology
FRS	Framingham Risk Score
MACEs	Major Adverse Cardiac Events
MI	Myocardial Infarction
PCE	Pooled Cohort Equation
RA	Rheumatoid Arthritis
RF	Rheumatoid Factor
SPSS	Statistical Package for Social Sciences
TASH	Tikur Anbessa Specialized Hospital
TNFi	Tumor Necrosis Factor inhibitors
WHO	World Health Organization

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Abstract

Background: Atherosclerotic cardiovascular disease (ASCVD) is the major cause of mortality in patients with Rheumatoid Arthritis (RA), due to the higher prevalence of conventional risk factors and other novel risk factors. This has been shown in the literature and the guidelines recommend a routine CV screening for all RA patients. Despite this, there is no formal cardiovascular risk assessment practice for our patients with Rheumatoid Arthritis and no studies have been published yet in Ethiopia and Africa that assessed the 10 year ASCVD risk score in this patient group.

Objectives: This study aimed to assess the ASCVD risk score among patients with RA on follow-up at the Rheumatology clinic of Tikur Anbessa Specialized Hospital, to correlate among AHA/PCE, WHO lab and non-laboratory CV risk assessment tools, to determine CV risk factors and assess statin use in high risk patients.

Methods: A single center cross-sectional study was conducted from September 1 to November 30, 2023 GC at the Rheumatology Clinic in Tikur Anbessa Specialized Hospital, Addis Ababa. A total of 180 patients were enrolled in the study and Data was collected through structured questionnaires using a standard WHO STEPs instrument for non-communicable Disease surveillance with some modifications. The updated 2019 WHO CVD risk charts and AHA/ACC PCE ASCVD plus score (2018) risk calculators were used to calculate the 10 year CVD risk score. Binary logistic regression was used to assess the association between high 10-year CVD risk and associated factors, with a p-value of <0.05 considered statistically significant

Results: The magnitude of high 10 year ASCVD risk score in RA patients was found to be 17.6% using the WHO non laboratory CV risk assessment tool which identified the higher proportion of high risk patients followed by AHA/PCE and WHO laboratory risk assessment tools which accounted for 8.3% and 2.8% respectively. Despite this discrepancy, there was a significant positive correlation among the three CV risk calculators with r (178) = .887 between WHO laboratory and non-laboratory CV risk tools, .863 between the WHO-non-laboratory and AHA/PCE risk tools and .915 among the WHO laboratory and AHA/PCE risk tools. Hypertension and age were found to be the main drivers of high 10 year ASCVD risk score and only 25% of the high risk groups were on statins. Dyslipidemia was the commonest CV risk factor identified followed by Hypertension and Diabetes Mellitus.

Conclusion and recommendations: The magnitude of elevated 10 year ASCVD score is high

among RA patients in Ethiopia which is demonstrated by the prevalent traditional CV risk factors. Despite this, Statin utilization among high risk patients is poor. We recommend a larger prospective observational study to identify RA specific variables and their association with cardiovascular disease. Primary care physicians and Internists have to practice routine ASCVD risk assessment for all patients with Rheumatoid Arthritis as per the guidelines. The WHO non-laboratory CV risk assessment chart can be a suitable tool in a resource limited setting like ours. Additionally, statins have to be administered for RA patients with intermediate and high CV risk.

Key words: ASCVD, Cardiovascular risk, Risk assessment, Rheumatoid Arthritis, Rheumatology clinic.

1. Introduction

1.1 Background

Rheumatoid arthritis is a chronic systemic autoimmune inflammatory disease which primarily affects the synovuim of the joints. It is characterized by chronic and destructive synovitis leading to irreversible joint damage and associated disability if left untreated, contributing for a significant morbidity. (1,2) The prevalence of RA varies throughout the world, but it is typically higher in industrialized nations. This difference in frequency can be attributed to a variety of causes, including genetics, exposure to environmental risk factors, and underreporting in other regions of the world. The estimated global burden of the disease is around 0.46% from a 2021 meta-analysis of 67 studies from 41 countries worldwide. (2) In contrast to the general population, a higher mortality rate is being recognized as a result of increased risk of cardiovascular disease, impacting the overall prognosis of patients with Rheumatoid Arthritis. (3)

1.2 Statement of the Problem

Atherosclerotic cardiovascular disease is the leading cause of death in patients with rheumatoid arthritis. (4) Both traditional and nontraditional risk factors such as inflammation and RA specific characteristics like disease activity, disease duration and RA treatment are reported to increase cardiovascular risk in these patients. (5, 6, 7)

According to a meta-analysis, people with RA have a 48% greater risk of acute CVD, compared to the general population, a 41% increased risk of stroke and 68% higher risk of myocardial infarction. (8)

An international study, A Trans-Atlantic Cardiovascular Consortium for Rheumatoid Arthritis, found that conventional Cardiovascular risk factors accounted for 49% of RA related CVD events, whereas disease specific characteristics including high disease activity, inflammatory markers, and antibodies accounted for 30%. This finding illustrates that the association between CV risk and RA extends beyond traditional risk factors. (9)

According to a large Danish cohort study, RA patients had a myocardial infarction risk that is comparable to individuals with Diabetes mellitus. Furthermore, it has been found that, the risk of MI in RA was almost 70% higher compared to the general population. (10)

There is scarcity in the literature regarding the prevalence of RA and its associated impacts in Africa. It is difficult to estimate the prevalence of RA in Ethiopia as there is no national registry but a study done in TASH showed a magnitude of 18.5% which accounted for a proportion of one fifth of the patients attending rheumatology clinic. (11) There is no study

regarding the burden of CVDs and CV risk assessment done in RA patients so far in Ethiopia.

1.3 Rationale of the study

It is well recognized that more than half of the cause of mortality in patients with RA is ASCVD which is attributed to both the prevalent traditional risk factors in this group of patients and the novel risk factors specific to Rheumatoid arthritis. (3) This has also been acknowledged by the 2016 EULAR task force which recommends screening, identifying CV risk factors and managing CVD risk in patients with inflammatory joint diseases. (12)

Studies mentioned in the literature review showed that screening and treatment (if indicated) for CV risk factors is poor despite the availability of tools incorporating CV risk of RA patients, resulting in undiagnosed and untreated risk factors. Therefore, it is essential to make an adequate CV risk assessment.

So far, there have been no studies that assessed the 10 year ASCVD risk in RA patients in Ethiopia. Additionally, patients are not routinely being assessed for CV risks at rheumatology clinic in TASH which is the only public rheumatology center that serves the whole population coming from different regions in the country.

This study will provide information regarding the 10 year ASCVD risk among RA patients on follow up at the rheumatology clinic and compare between two different risk score calculators. The results will provide input to primary care physicians and the rheumatology unit in maximizing care for patients with RA and for researchers in future studies to be used as a pilot study to further broaden the risk assessment in RA patients using imaging modalities to identify subclinical atherosclerosis. The results of the study will reach to the beneficiaries through presentations to the department of internal medicine of Addis Ababa University, College of health sciences and through publication in a reputable journal.

2. Literature Review

2.1 Epidemiology: Worldwide, Africa, Ethiopia

Rheumatoid arthritis is the most prevalent systemic autoimmune disease among the rheumatic inflammatory musculoskeletal diseases. It is a major global public health challenge; however the burden of the disease varies geographically.(13)

Worldwide, according to the Global burden of Disease study in 2017, the prevalence of RA was estimated to be 0.27%(13) which has doubled in a meta-analysis study done in 2021.(2) There have been 7.4% and 8.2% increase in the age-standardized point prevalence and annual incidence rates of RA since 1990, respectively, leading to greater disability adjusted life year (DALY) rates with minor geographical variations. (13)

Regarding Africa, there are regional differences in the prevalence, but according to the 2017 Global Burden of Disease study, with a comparable trend in the incidence (37 per 100,000 patient-years in North Africa and the Middle East and 23 per 100,000 patient-years in Western Sub-Saharan Africa), higher estimations were recorded in North Africa and the Middle East (0.26%) as opposed to Western sub-Saharan Africa (0.14%). (13)

In Ethiopia, it is common to encounter patients with musculoskeletal symptoms but there are no published articles or studies so far which assessed the burden of Rheumatoid Arthritis in the country.

2.2 Cardiovascular disease risk in RA

Evidences show that high CVD risk in patients with RA is not only related to the prevalent traditional CV risk factors but also the presence of novel risk factors which include inflammation, presence of carotid plaques, seropositivity (RF and ACPA), extra-articular RA manifestations and functional disability.(5,6)

The increased risk is acknowledged in the guidelines and has been implemented in several risk calculators. However, screening is poor in clinical practices. In a study on general practitioners (GPs) and the cardiovascular risk associated with RA patients, it was discovered that most did not do the necessary screening exams and did not acknowledge RA as a separate CV risk factor.(14) A different study discovered that just one-third of individuals whose risk assessment indicated they should get treatment were appropriately managed. (15)

2.3 Traditional risk factors

The significant impact of traditional cardiovascular risk variables in people with RA to total CVD risk is shown in a meta-analysis that showed those with concurrent Diabetes and hypertension had 89% and 84% greater risk of MI, respectively, compared with those without these risk factors. It has also been shown that a high prevalence of CVD related morbidity was observed in RA patients with Hypertension, Type 2 diabetes mellitus, smoking, hypercholesterolemia and obesity.(16) An international study also revealed that 49% of CVD events in RA were attributed to traditional CVD risk factors (in particular, smoking and hypertension).(9)

Similarly, in another study, Hypertension is found to be more common in RA with a prevalence of 57%. It has also been demonstrated that people with RA frequently have other conventional risk factors, but are underdiagnosed and inadequately managed.(17). In a different study, an increase in SBP of 1-5mmHg was associated with a significant event rates of coronary artery disease and stroke in one year in RA patients.(50)

Smoking, which is one of the modifiable CV risk factors of particular importance in patients with RA, has been linked to progression of RA disease activity and reduced medication efficacy.(18)

Another well-known CVD risk factor with intriguing effects on RA and CVD is Dyslipidemia. However, poorly treated RA is associated with a paradoxical reduction in lipid levels despite substantial ongoing CVD risk from ongoing concurrent inflammation.(19) For this reason, EULAR encourages the use of the total cholesterol/high-density lipoprotein (HDL) ratio, which is a better CVD risk predictor in RA than individual lipid components.(12)

On the contrary, regarding obesity which is another CV risk factor, an antagonistic association between BMI and mortality in RA patients is seen. According to a study, weight loss is a reliable predictor of mortality in RA, with a decline in BMI of more than or equal to 1 kg/m2 being linked to a nearly doubled risk of death. This association is explained by unintentional weight loss that occurs during active inflammatory condition. (20)

From the non-modifiable CV risk factors, age contributes for a higher 10 year risk of ASCVD which is demonstrated in a population based inception cohort study in Minnesota, where aging increased the predicted CVD risk exponentially. It has also shown that the presence of RA specific risk factor, specifically RA seropositivity was associated with doubling the effect of age on 10 year CV risk.(49)

2.4 Rheumatoid Arthritis Disease-Specific Factors

Studies demonstrate that CV mortality is elevated in RA, ranging from 43%-66% greater than the general population, even after adjusting for age, gender, and other conventional cardiovascular risk factors.(22) This is due to the fact that, in addition to the traditional CVD risk factors, disease- specific factors also significantly contribute to CVD risk in RA. Given that RA and atherosclerosis both have similar underlying inflammatory mechanisms, studies have linked RA's higher cumulative inflammatory burden to an elevated risk of CVD.(21)

Measuring indicators of inflammation has been suggested as a strategy to enhance the prediction of the risk of CV events as inflammation is considered to have a part in the pathophysiology of cardiovascular events. According to a study published in New England Journal of Medicine, the strongest univariate predictor of the risk of cardiovascular events was hs-CRP.(23) In another study, Statin therapy is associated with a significant reduction in CV events in patients with elevated hs-CRP irrespective of the level of LDL cholesterol.(24)

It has been demonstrated that both disease duration and disease activity influence the development of carotid atherosclerosis. They are also associated with plaque size and vulnerability in patients with RA. Therefore, screening by ultrasound of the carotid arteries on asymptomatic patients adds value for the evaluation of CVD risk by reclassifying a significant portion of RA patients into a more suitable CVD risk group.(25) According to one cohort study, patients with RA who have carotid plaques have a higher risk of developing acute coronary syndrome(ACS) with a rate of 1.1 per 100 person-years for those without plaques and 4.3 per 100 person years for those with bilateral plaques.(26)

In the contrary, one study found that regardless of the disease duration, a 1 unit increase in the DAS 28 score was associated with a 28% increase in CV risk, suggesting that disease activity as well as the frequency and duration of flares over time may contribute to higher CVD risk in RA.(27) Similarly, in a large-scale research conducted in 2015, a 10-point decline in the CDAI (Clinical disease activity index) led to a 26% decrease in CV events.(28)

Seropositivity, including the presence of rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) positivity is linked to a more severe disease activity, higher CV mortality, and may even speed the atherosclerotic process.(29)

2.5 CV Risk Assessment

In its most recent guideline, the European League Against Rheumatism (EULAR), suggests screening every RA patient at least every five years and more frequently if an elevated CV risk was previously identified. The majority of risk calculators do not incorporate the disease specific risk variables as risk indicators, which may underestimate the genuine CVD risk in patients with RA. (12). Thus, the most evidence-based method currently available for estimating CVD risk in patients with RA is to modify general population CVD risk algorithms in accordance with national guidelines, giving all patients with RA a 1.5 multiplication factor, with the exception of QRISK 2, where RA is included as a risk variable in the risk score. (12)

According to one study, many RA patients still appear to have their risk underestimated by these calculators especially those who are categorized as low and intermediate risk. And only a small percentage of patients are transferred to a higher risk category by using the multiplication factors. (1)

In a study conducted in India, out of 332 patents with RA, 12% had diabetes mellitus, 21.4% had hypertension, and 6.9% had ever smoked or were current smokers. The proportion of RA patients with estimated 10-year CVD risk >10% ranged from 16.2 to 41.9% between scores with the highest risk indicated by FRS. With Q-RISK 2, which uses RA as an indicator for CVD risk, 31.9% of them had a 10 year CVD risk of >10%. It was also found to have the highest association with higher CIMT. The same study found that 24.8% of the high risk groups were not taking statins. (30)

According to a study conducted in Mexico on 116 patients, 23.2%, 16.3%, and 9.4% of RA patients were categorized as high risk based on the ACC/AHA 2013, FRS BMI, and QRISK 2 risk scores. The lipid paradox in RA patients is thought to be the reason why FRS LIPIDS classified only 5.1% of the patients as high risk. Regarding CV risk factors, 12.1% had Type 2 Diabetes, 32.8% had hypertension, 8.6% actively smoked, and 27.6% had dyslipidemia. Furthermore, just 14.7% of the high-risk groups were taking statins. (31)

In a different study done in Mexico, 9.3% of the 97 patients were current or past smokers, 33% had been diagnosed with Hypertension and were on anti hypertensives, 28.9% had dyslipidemia, and 13.4% had Type 2 diabetes. It is shown that Framingham lipids, Framingham BMI, and QRISK2 risk calculators had the highest sensitivity and specificity for diagnosis which correlates best with carotid ultrasound results.(32)

In an Italian study which included 84 patients with RA, 39.3%, 19.0%, 28.6%, 29.8% and 39.3% of them were classified as having high CVD risk according to ACC/AHA 2013,

mSCORE, FRS BMI, QRISK3 and ERS-RA respectively. The latter is a disease specific CV risk prediction score that includes a number of RA-specific parameters including corticosteroid use, disease duration and disease activity. All were found to match well with carotid artery ultrasound findings. (33)

According to a Dutch study that used a Dutch SCORE table to evaluate the 10 -year ASCVD risk in RA patients, a total of 17% had a low risk, 21% had an intermediate risk, and 53% had a high risk. Additionally, only 18% of the high-risk groups received sufficient treatment for their CV risks. (34)

2.6 CV Risk Management

There are two main approaches in managing CV risk in RA patients. These include pharmacological and non pharmacological management of traditional risk factors as well as tight control of disease activity with disease modifying Anti Rheumatic medications.

Lifestyle measures, including smoking cessation and engaging in regular physical exercise reduce CVD risk in inflammatory joint diseases. A number of cardiovascular advantages of exercise have been linked to RA, including reduced cardiovascular risk, improved cardiorespiratory fitness, and improved micro and macrovascular function. (35)

Regarding treatment targets for lipid levels and blood pressure in RA patients, there is no difference from the general population. Data from population statistics has demonstrated a systolic blood pressure reduction of 10 mmHg is linked to a 20% decrease in CVD occurrences. (12, 36)

The Trial of Atorvastatin for the Primary Prevention of Cardiovascular Events in Patients with Rheumatoid Arthritis showed that statin medication was beneficial in reducing the risk of CVD in RA patients, with a substantial decrease in the LDL-C level.(38) Similarly, major adverse cardiovascular events (MACEs) are reduced by about 20% with a 1-mmol/L drop in LDL cholesterol with statin use. (37)

Treatment with DMARDs especially Methotrexate (MTX), and biological DMARDs (bDMARDs), including TNF inhibitors (TNFi) reduce the disease activity and significantly lower the risk of Cardiovascular disease (CVD) in RA patients. In a meta-analysis, methotrexate has been associated with a decrease in all-cause and CVD mortality in RA patients. It led to a 21% lower risk of overall CVD and an 18% lower risk of MI in those with inflammatory arthritis. (39)

NSAID use in RA should be done so with caution, especially in patients who have known CVD or who have CVD risk factors. Diclofenac and other non-selective NSAIDs, according to a new meta-analysis, had negative impact on CVD outcomes in RA patients (40) whereas, no increased risk of serious CV events was seen in RA patients taking naproxen in a well conducted meta-analysis. (41)

Regarding use of corticosteroids, there are conflicting views in RA patients. By lowering inflammation and enhancing mobility, the advantage of reducing high-grade inflammation may outweigh the negative CVD effects of corticosteroid use. In the contrary, according to studies, they increase the risk of CVD in a dose- and time-dependent manner. A comparatively high daily dose (i.e., >8 mg/day), a high cumulative dose, and a prolonged exposure to corticosteroids (in years) appear to be associated with an elevated risk of CVD. (42) As a result, it is recommended to treat active RA for the shortest amount of time with the lowest therapeutic dose of corticosteroids. (12)

2.7 Conceptual Framework

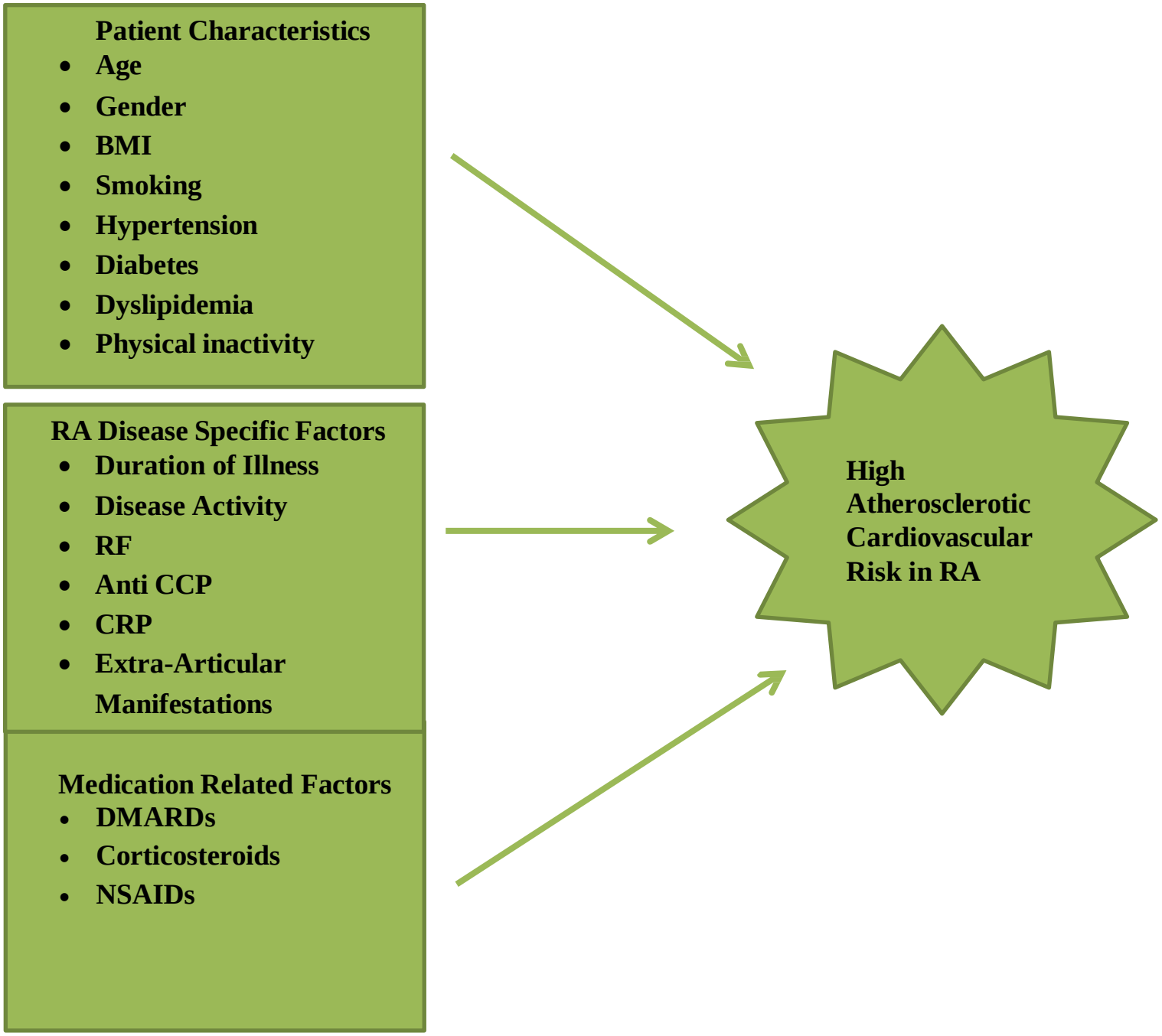


Figure 1: Conceptual Framework of factors affecting the risk of Atherosclerotic cardiovascular disease, developed based on literatures

3. Objectives of the study

3.1 General Objective

- To assess the 10 year ASCVD risk and its associated factors among patients with Rheumatoid arthritis

3.2 Specific objectives

- To assess the 10 year ASCVD risk score among patients with Rheumatoid arthritis
- To determine the correlation among WHO laboratory, non-laboratory and AHA/PCE CV risk assessment tools
- To identify CVD risk factors among patients with Rheumatoid arthritis at TASH on follow up at rheumatology clinic
- To identify factors associated with high 10 year ASVD risk score in patients with RA at TASH on follow up at rheumatology clinic
- To assess utilization of statin in high risk group RA patients

4. Methods

4.1 Study area

The study was conducted at the Rheumatology referral clinic in Tikur Anbessa Specialized Hospital which is the largest and the pioneer referral hospital in Addis Ababa, the capital city of Ethiopia. It is an institution where specialized clinical services are rendered to the whole nation and with more than 700 beds for inpatient services. It is also the main teaching hospital for the College of Health Sciences at Addis Ababa University.

Rheumatology clinic is one of the sub-specialty clinics in the hospital and functions as the only public rheumatology center for the whole nation. It is led by 2 Rheumatologists and provides service on two working days per week with an average of 550 cases seen per month.

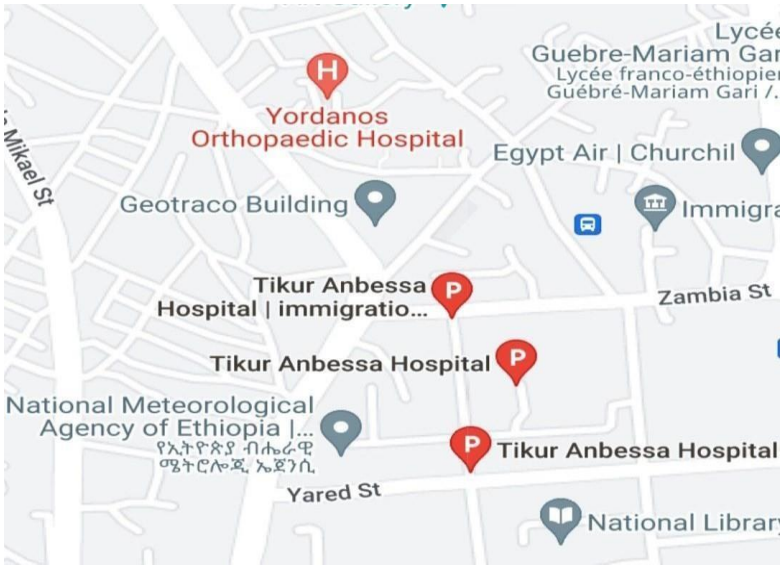


Figure 2**:** Map of Tikur Anbessa Specialized Hospital

4.2 Study period

The study was conducted from September 1- November 30, 2023GC at the Rheumatology referral clinic at Tikur Anbessa Specialized Hospital.

4.3 Study design

An institution-based Cross-sectional study design was used.

4.4 Population

4.4.1 Target Population

All RA patients in Ethiopia

4.4.2 Source Population

All patients who were diagnosed with Rheumatoid Arthritis and visited the Rheumatology clinic of Tikur Anbessa Specialized Hospital from September 1 to November 30, 2023 GC, for follow up. A total of 570 patients visited the Rheumatology clinic.

4.4.3 Study Population

All RA patients who met the inclusion criteria.

4.5 Inclusion and exclusion criteria

4.5.1 Inclusion criteria

- Age between 40-74 years on follow up at the Rheumatology referral clinic for atleast 3 months
- Those with complete biochemical tests (FBS, LIP) and CRP levels

4.5.2 Exclusion criteria

- Patients with established ASCVD
- Patients with overlap syndromes (Connective tissue disorders apart from RA)
- Those who are critically ill during data collection

4.6 Sample size and sampling techniques

Sample size determination:

The sample size was determined by using a single population proportion formula. Prevalence of 50% high risk ASCVD risk score was used as no studies were done in Ethiopia or Africa. N(population of 342) was used from an average of 190 cases of RA who visit the Rheumatology clinic monthly (taken from a monthly outpatient department audit reports of the 3 consecutive months prior to data collection, of which 60% of RA patients were above the age of 40).

The sample was calculated by assuming a Confidence interval of 95%, 5% margin of error, & 10% non-response rate.

$$\text{Sample size} = \frac{\frac{z^2 \times p(1-p)}{e^2}}{1 + \left(\frac{z^2 \times p(1-p)}{e^2 N}\right)}$$

where;

Z= Z-score for 95% confidence interval=1.96 P=Population proportion = set to 50%

e= margin of error= 5%

So, $n = \frac{(1.96)^2 \times (0.5)(1-0.5)}{(0.05)^2} = \frac{0.9604}{0.0025}$

$= \frac{384.16}{1 + 1.12} = \frac{384.16}{2.12} = 181.2 \sim \mathbf{181}$

$1 + \frac{(1.96)^2 \times (0.5)(1-0.5)}{(0.05)^2 \times 342} = 1 + 0.9604 = 0.855$

Using a 10% non-response rate: 181+18=**199**

Sampling procedures:

Consecutive sampling technique was used. All subjects who met the inclusion criteria were included in the study. A total of 180 study participants were enrolled in the study with a response rate of 90.5%.

4.7 Study variables

4.7.1 Dependent variable

- High 10 year ASCVD risk score
- Statin use among intermediate and high risk RA patients

4.7.2 Independent variables

- Socio-Demographic Variables: Age, Sex, Educational Status, Marital Status, Occupation, Household Income, Residence
- Behavioral Variables: Smoking Status(Previous/Current), Alcohol Use, Physical

Activity Level

- Clinical Variables: Blood Pressure, BMI, History And/or Diagnosis of Hypertension(And Use Of Antihypertensive), History And/or Diagnosis of Diabetes(Use of Anti- Diabetics), Dyslipidemia, RA Disease Activity, Disease Duration, Use Of DMARDs, Steroids, NSAIDs
- Laboratory Variables: FBS/Hga1c, Lipid Profile, RF, Anti CCP Antibody, CRP

4.8 Operational definitions

- **RA**: defined by the 2010 ACR/EULAR classification criteria: a total score of atleast 6 from the individual scores in four domains (51)
  - Number and site of involved joints: 2 - 10 large joints= 1 point
    1 - 3 small joints=2 points
    4 - 10 small joints=3 points
    >10 joints=5 points
  - Abnormal serology tests (RF or anti CCP antibody)
    Low positive=2 points
    High positive (greater than 3x the ULN)=3 points
  - High acute phase reactants(ESR/CRP above the ULN)=1 point
  - Duration of symptoms (≥6 weeks)=1 point

OR

Presence of radiological evidence of RA for those who do not fulfill the above criteria

- **ASCVDs**: include

- Coronary artery disease: fatal or nonfatal myocardial infarction (MI), angina pectoris, and/or heart failure
- Cerebrovascular disease: fatal or nonfatal stroke and transient ischemic attack
- Peripheral artery disease: intermittent claudication and critical limb ischemia
- Aortic atherosclerosis and thoracic or abdominal aortic aneurysm

- **ASCVD risk calculators** -.are multivariate risk models that, by evaluating a number of variables, have been constructed to estimate the probability of early ASCVD events in people who are healthy and asymptomatic.

- **Risk prediction models**:
  - WHO 2019 Updated CVD risk charts (WHO Hearts risk charts): regional based charts to assess 10 year CVD risk in patients aged between 40-74 years(48)
    - Laboratory based (includes FBS & Total Cholestrol level)

Classifies the risk as: Low risk ≤ 10%,

Intermediate risk between 10 – 20%

High risk ≥ 20%.

- Non-laboratory based (includes only clinical parameters)

  Classifies the risk as;

  Low risk ≤ 10%, and High risk >10%.

- AHA/ACC PCE ASCVD plus score (2019): calculates 10 year risk in Patients aged 40-79 years without ASCVD. (45)

  Classifies the risk into:

  Low risk <5%;

  Borderline risk 5%-7.5%;

  Intermediate risk 7.5-20%, and

  High risk ≥20%

- Indications for Statin use as primary prevention are as follows(45)
  - WHO risk score ≥ 20% (WHO/ISH 2019 updated guideline)(48)
  - Intermediate risk scores with enhancing factors (like RA)
  - DM between 40 – 75 years, LDL 70 – 189mg/dl, irrespective of CVD risk score
  - LDLc ≥190mg/dl
  - non Dialysis requiring CKD ≥ 50 years
- **Dyslipidemia**: ATP III definition(46)

  LDL≥130mg/dl, >100mg/dl(for patients with Diabetes Mellitus) HDL<40mg/dl for males, <50mg/dl for females, Total cholestrol≥200mg/dl, Triglycerides≥150mg/dl
- **Hypertension**: defined according to the 2023 ESH guidelines for the management of arterial Hypertension(47) with two repeat measurements at the Rheumatology referral clinic and/or the presence of previously known history of hypertension
- Diabetes Mellitus: FBS>125 mg/dl and/or previous known history of Diabetes Mellitus and/or documented use of insulin/oral hypoglycemic agents.

4.9 Data collection procedures

4.9.1 Data collection tools

Data collection was conducted by using a standard questionnaire tool adapted from WHO STEPs instrument used for surveillance of non-communicable diseases **with some modifications.** The STEPS instrument is comprised of three different levels or "steps" of risk factor assessment: Step

1 (questionnaire), Step 2 (physical measures) and Step 3 (biochemical measures). (44)

The Questionnaire was written in English with translation into local language by interviewers. It included;

Socio-demographic characteristics (Age, Gender, Religion, Address, Marital Status, Educational Level, Occupation, and Monthly Income),

Behavioral factors (current/previous smoking history, alcohol consumption, and physical activity). Since none of the study participants reported alcohol intake, it was not included in the analysis.

Clinical characteristics (History of Hypertension and anti hypertensives, DM and anti diabetic medications, use of statins. Modifications added to the components of clinical characterstics in the Standard Questionnaire included RA specific parameters (Duration of illness, disease activity, use of DMARDs, NSAIDs, corticosteroids).

Physical measures (BP and BMI). Blood Pressure was obtained using a Digital Sphygmomanometer for all participants. Patients were then categorized as having hypertension or not based on the 2020 ISH/2018 ESC Blood pressure category after two repeat measurements.

Biochemical measurements (CRP, FBS and lipid profiles) for all study participants and serological tests(RF and anti-CCP) were collected for the available ones. Recent Laboratory parameters (with in the past 3 months) were collected from the laboratory I care system (Electronic medical recording system of TASH).

The 10-year ASCVD risk score was calculated by using the WHO CVD risk charts (laboratory and non-laboratory based) and AHA/ACC PCE ASCVD plus for all study participants. For each scoring result, a 1.5 multiplication factor was used according to the recommendations.

4.9.2 Data collection method

Data was collected from RA patients who consented and fulfilled the inclusion criteria by 3 well trained General Practitioners under the supervision of the principal investigator. The data collection was made by kobotoolbox standard data collection tool https://www.kobotoolbox.org/.(43)

Through a review of electronic medical records, information about the participants' clinical and laboratory profiles was acquired. During the appointment, all clinical records that were lacking were gathered.

4.9.3 Data management

a) Data quality control

The questionnaire on the Kobotoolbox was reviewed for completeness and pre test was done on 5% of the sample which are not included in the study. Onsite training was also given for the data collectors to ensure consistency. Each Question on the KoboToolBox was made mandatory and filled data was being checked daily for completeness and consistency by the Primary investigator.

b) Data processing and analysis

The data was obtained from Kobotoolbox in Excel format after being verified as complete, and then it was exported into the IBM/SPSS 26th edition for analysis. The data was cleaned for inconsistency and was made ready for analysis. The dependent & independent variables were categorized using traditional clinical categories.

Socio-demographic, Behavioral, Clinical, and Laboratory parameters were summarized with descriptive statistics. Categorical variables were presented with frequencies and percentages and were compared with chi-square test of independence. Continuous variables were described with mean (standard deviation) and median (interquartile range) according to their distribution pattern. Mann-Whitney U and independent sample t-test were used for non-normally and normally distributed continuous predictors.

Univariate analysis was performed to screen out potentially significant independent variables at 25% level of significance. Factors related with high 10 year ASCVD risk score based on the WHO non-laboratory CV risk tool were included in a bivariate and subsequent multivariable binary logistic regression analyses to identify factors associated with high 10-year ASCVD risk. The assumption of multicollinearity was checked using VIF and the adequacy of the final model was checked using the Hosmer and Lemeshow goodness of fit test where p value of >0.05 indicate that the final model fitted for the data well. Variables with p-value ≤0.05 were considered as statistically associated with the outcome variable.

WHO Non-laboratory, WHO laboratory, and AHA 10-year CV risk assessment scores were compared to each other using Spearmans rank Correlation.

The secondary outcome (utilization of statins for intermediate and high risk groups) was assessed and compared among WHO laboratory, WHO Non-laboratory, and AHA/PCE 10-year CV risk assessment tools as well as with possible determinants of higher risk categories. The analysis was conducted after dichotomizing all three tools while considering indication for statin use.

4.10 Ethical consideration

For every subject, verbal informed consent was obtained. A sufficient description of the study's objective and the participants' right to refuse participation or to withdraw if they were unwilling were provided, and this was ensured.

Personal identifier information was not included in the questionnaire, rather codes were used. Filled questionnaires were stored safely by the primary investigator.

The study protocol was submitted and approved by the Institution review board(IRB), ethical review committees of the Department of Internal Medicine, College Of Health Sciences, Addis Ababa University.

4.11 Plan for Dissemination of the results

The result of this study will be presented to the Department of Internal Medicine, and reach to the beneficiaries through presentations, scientific conferences and publications.

5. Results

The analysis included 180 RA patients from a sample size of 199 (with 90.5% response rate) who had follow up for at least 03 months and visited the Rheumatology referral clinic of Tikur Anbessa Specialized Hospital from September 1 to November 30, 2023 GC. The majority of study participants were females which accounted for 90.6% (163). Age ranged from 40 to 74 y with median (IQR) of 50 (44 – 60). The sample constituted 16.1% (29) patients who had no formal education while 26.1% (47) have attended higher education. The marital status of studied patients indicated that more than half were married while 46% (83) were single, divorced, or widowed.

The permanent area of residence for the majority of the study participants was Addis Ababa which accounted for 77.2% (139). Majority of the study group were unemployed 46.1% (83) and 38.3% (69) have reported to have no established source of monthly income. A significant proportion of studied patients reported to have never smoked tobacco accounting for 98.3% (177) and 95.6% (172) had sedentary life style.

The Body Mass Index (BMI) of the study participants ranged from 15 to 39 with Mean (SD) of 25(5) whereas it ranged from 18.5 to 24.9 kg/m^2 in 49.4% (89) of the participants. Hypertension accounted for 40.6% (73) of the sample whereas only 39 (53.4%) were on anti-hypertensive treatment. Diabetes mellitus and Dyslipidemia accounted for 16.1% (29) and 53.9% (97) of the sample respectively. The majority of patients with diabetes are on treatment which accounted for 82.3% (24). Among Hypertensive patients 45 (57%) and 15 (19%) had concomitant Diabetes and Dyslipidemia respectively. The sample consisted of 3.9% (7) patients with Chronic Kidney Disease (CKD) and 2.8% (5) patients living with HIV.

Almost all the studied participants (99.4%) were on Disease Modifying Anti-Rheumatic Drug (DMRAD) therapy. The most commonly used DMARD was Methotrexate in 88.9%(160) followed by Chloroquine in 31.7%(57). The majority of patients were on Methotrexate monotherapy 67.6%(121) followed by Methotrexate and Chloroquine combination therapy in 22.3%(40) of the participants. The Disease Activity of RA as measured by DAS-28 CRP Score (DAS), 64.4% (116) and (17.8%) 32 patients were in remission and in low disease activity whereas 17.2% (31) and only 0.6% (1) had moderate (2.6 – 3.2), and severe (> 5.1) disease activity scores respectively. Similarly, the Clinical Disease Activity Index (CDAI) categorized most of the study participants in remission and low disease activity which accounted for 37.2% (67) and 36.1% (65) respectively.

23.3% (42) and 3.3% (6) patients had moderate (10.1 to 22), and severe (>22) disease activity based on the CDAI respectively. Patients who had extra-articular manifestations of Rheumatic Arthritis account for 5% (9).

Oral Non-inflammatory Anti-inflammatory Drugs (NSAIDS) use was reported by 31.7% (57) patients while 68.3% (123) were on steroids, particularly on prednisolone. The daily dose of prednisolone of 20.3% (25) was greater than 7.5 milligrams.

The laboratory data of studied patients during the study period showed 25% (42) patients had C-reactive Protein (CRP) level of 4 to 10 mg/dl and 2(1.1%) had values above 10 mg/dl. For the majority of patients, anti-CCP status was not determined 83.9% (151) and 62.1%(18) patients had positive anti-CCP results. Serum Rheumatoid Factor was determined for 53.3% (96) patients out of which 55.3% (55) had positive results. Serum lipid profile of the study group indicated that 25.6% (46), 31.7% (57), 12.2% (22), 13.9% (25), have high total cholesterol, LDL, and triglyceride, and low HDL levels respectively.

Table 1: Socio-demographic characteristics of study participants by high-10 year CV risk categories classified with WHO non-laboratory and AHA CV risk assessment tools

Characteristics	Sample n(C%)	10-Year High ASCVD Risk, n(R%)		p* value
		WHO	AHA	
Study Participants	180 (100.0)	32 (17.8)	15 (8.3)	NA
Gender				
Male	17 (9.4)	7 (41.2)	6 (35.3)	.008
Female	163 (90.6)	25 (15.3)	9 (5.5)	
Age Median (IQR)	50 (44 – 60)	48 (43 – 54)	65 (61 – 70)	.000
Age group				
40-50	94 (52.2)	0 (0.0)	0 (0.0)	.000
51-60	50 (27.8)	7 (14.0)	2 (4.0)	
61-70	32 (17.8)	21 (65.6)	10 (31.3)	
>70	4 (2.2)	4 (100.0)	3 (75.0)	
Level of Education				
No formal education	29 (16.1)	9 (31.0)	2 (6.9)	.132
Primary school	70 (38.9)	8 (11.4)	2 (2.9)	
Secondary school	34 (18.9)	7 (20.6)	5 (14.7)	
Higher education	47 (26.1)	8 (17.0)	6 (12.8)	
Marital Status				
Single	33 (18.3)	3 (9.1)	0 (0.0)	.125
Married	97 (53.9)	15 (15.5)	10 (10.3)	
Divorced/separated	23 (12.8)	6 (26.1)	3 (13.0)	
Widowed	27 (15.0)	8 (29.6)	2 (7.4)	
Address of Residence				
Out of Addis Ababa	41 (22.8)	7 (17.1)	3 (7.3)	.571
Addis Ababa	139 (77.2)	25 (18.0)	12 (8.6)	
Occupation				
Government employee	38 (21.1)	2 (5.3)	2 (5.3)	.000
Private corporations	10 (5.6)	1 (10.0)	1 (10.0)	
Self employed	26 (14.4)	1 (3.8)	0 (0.0)	
Unemployed/supported	83 (46.1)	13 (15.7)	6 (7.2)	
Retired	23 (12.8)	15 (65.2)	6 (26.1)	
Income (ETB)				
No income	69 (38.3)	12 (17.4)	6 (8.7)	.635
<5000	74 (41.1)	16 (21.6)	6 (8.1)	

5,000-10,000	31 (17.2)	4 (12.9)	3 (9.7)
>10,001	6 (3.4)	0 (0.0)	0 (0.0)

Abbreviations: C% - Column %, R% - Row %, WHO – World Health Organization, AHA – American Heart Association, ASCVD – Athero-sclerotic Cardio-vascular Disease, CV – Cardio-vascular, ETB – Ethiopian Birr

*p values are for chi-square test of independence with WHO non-laboratory risk classification categories except Age (Mann-Whitney U test)

Table 2: Behavioural and Clinical parameters of study participants and high 10 year CV -risk categories classified with WHO non-laboratory and AHA CV risk assessment tools

Characteristics	**Sample, n(C%)**	**10-Year High ASCVD Risk, n(R%)**		**p* value**
		WHO	**AHA**	
Smoking Status				
Never smoked	177 (98.3)	30 (16.9)	13 (7.3)	.047
Previous smoker	2 (1.1)	1 (50.0)	1 (50.0)	
Current smoker	1 (0.6)	1 (100.0)	1 (100.0)	
Physical Activity				
Sedentary	172 (95.6)	30 (17.4)	14 (8.1)	.675
Moderate physical activity	7 (3.9)	2 (28.6)	1 (14.3)	
Vigorous physical activity	1 (0.6)	0 (0.0)	0 (0.0)	
BMI, kg/m^2, Mean(SD)	25 (5)	25 (5)	26 (4)	.431
BMI Categories				
< 18.5	11 (6.1)	0 (0.0)	0 (0.0)	.321
18.5 - 24.9	89 (49.4)	18 (20.2)	8 (9.0)	
25 - 29.9	55 (30.6)	11 (20.0)	4 (7.3)	
30 and above	25 (13.9)	3 (12.0)	3 (12.0)	
Comorbidities				
Hypertension	73 (40.6)	23 (31.5)	14 (19.2)	.000
Hypertension on Rx	39 (21.7)	11 (28.2)	10 (25.6)	.054
Diabetes Mellitus	29 (16.1)	5 (17.2)	6 (20.7)	.934
Diabetes on Rx	24 (13.3)	4 (16.7)	6 (25.0)	.878
Dyslipidaemia	97 (53.9)	17 (17.5)	11 (11.3)	.924
High TC	46 (25.6)	7 (15.2)	2 (4.3)	.599
High LDL	57 (31.7)	9 (15.8)	6 (10.5)	.635
Low HDL	25 (13.9)	3 (12.0)	2 (8.0)	.415
High TG	22 (12.2)	2 (9.1)	2 (9.1)	.255
HIV	5 (2.8)	0 (0.0)	0 (0.0)	.292

CKD	7 (3.9)	2 (28.6)	1 (14.3)	.446
Types of DMARDs used				
Methotrexate	160 (88.9)	30 (18.8)	13 (8.1)	.335
Chloroquine	57 (31.7)	9 (15.8)	4 (7.0)	.635
Sulfasalazine	1 (0.6)	0 (0.0)	0 (0.0)	.641
DAS 28 CRP				
<2.6(in remission)	116 (64.4)	21 (18.1)	8 (6.9)	.371
2.6-3.2(low disease activity)	32 (17.8)	3 (9.4)	3 (9.4)	
3.21-5.1(moderate disease activity)	31 (17.2)	8 (25.8)	4 (12.9)	
>5.1(severe disease activity)	1 (0.6)	0 (0.0)	0 (0.0)	

Abbreviations: C% - Column %, R% - Row%, BMI – Body Mass Index, M (SD) – Mean (Standard Deviation), M (IQR) – Median (Interquartile Range), Rx – Treatment, RA – Rheumatoid Arthritis, DMARD - Disease Modifying Anti Rheumatic Drugs, DAS – Disease Activity Score

*p values are for pearson's chi-square test of independence except Duration of RA (Mann-Whitney U test) and BMI (independent sample t-test)

Table 2 (continued)

Behavioural and Clinical parameters of study participant and 10-year high-risk categories classified with WHO non-laboratory and AHA CV risk assessment tools

Characteristics	Sample	10-Year High ASCVD Risk		p value
		WHO	AHA	
CDAI				
</=2.8(in remission)	67 (37.2)	10 (14.9)	4 (6.0)	.434
2.81-10(low disease activity)	65 (36.1)	12 (18.5)	5 (7.7)	
10.1-22(moderate disease activity)	42 (23.3)	10 (23.8)	5 (11.9)	
>22(severe disease activity)	6 (3.3)	0 (0.0)	1 (16.7)	
NSAID use	57 (31.7)	12 (21.1)	5 (8.8)	.434
Steroid use	123 (68.3)	22 (17.9)	7 (5.7)	.955
Dose of Prednisolone				
<7.5 mg/day	98 (79.7)	17 (17.3)	5 (5.1)	
7.5-40 mg/day	25 (20.3)	5 (20.0)	2 (8.0)	
40 mg/day and above	0 (0.0)	0 (0.0)	0 (0.0)	
Extra-articular Manifestations	9(5)	1 (11.1)	0 (0.0)	.690
CRP				
3 mg/dl and less	133 (73.9)	19 (14.3)	10 (7.5)	.084
4-10 mg/dl	45 (25.0)	12 (26.7)	5 (11.1)	
>10mg/dl	2 (1.1)	1 (50.0)	0 (0.0)	
Anti CCP (n = 29)				
Positive	18 (62.1)	2 (11.1)	0 (0.0)	.515
Negative	11 (37.9)	1 (9.1)	0 (0.0)	
RF (n = 97)				
Positive	55 (57.3)	7 (12.7)	4 (7.3)	.499
Negative	41 (42.7)	8 (19.5)	4 (9.8)	

Table 2 (continued)

Behavioural and Clinical parameters of study participant and 10-year high-risk categories classified with WHO non-laboratory and AHA CV risk assessment tools

Characteristics	Sample	10-Year High ASCVD Risk		p value
		WHO	AHA	
CDAI				
</=2.8(in remission)	67 (37.2)	10 (14.9)	4 (6.0)	.434
2.81-10(low disease activity)	65 (36.1)	12 (18.5)	5 (7.7)	
10.1-22(moderate disease activity)	42 (23.3)	10 (23.8)	5 (11.9)	
>22(severe disease activity)	6 (3.3)	0 (0.0)	1 (16.7)	
NSAID use	57 (31.7)	12 (21.1)	5 (8.8)	.434
Steroid use	123 (68.3)	22 (17.9)	7 (5.7)	.955
Dose of Prednisolone				
<7.5 mg/day	98 (79.7)	17 (17.3)	5 (5.1)	
7.5-40 mg/day	25 (20.3)	5 (20.0)	2 (8.0)	
40 mg/day and above	0 (0.0)	0 (0.0)	0 (0.0)	
Extra-articular Manifestations	9(5)	1 (11.1)	0 (0.0)	.690
CRP				
3 mg/dl and less	133 (73.9)	19 (14.3)	10 (7.5)	.084
4-10 mg/dl	45 (25.0)	12 (26.7)	5 (11.1)	
>10mg/dl	2 (1.1)	1 (50.0)	0 (0.0)	
Anti CCP (n = 29)				
Positive	18 (62.1)	2 (11.1)	0 (0.0)	.515
Negative	11 (37.9)	1 (9.1)	0 (0.0)	
RF (n = 97)				
Positive	55 (57.3)	7 (12.7)	4 (7.3)	.499
Negative	41 (42.7)	8 (19.5)	4 (9.8)	

The 10-year Cardio-vascular (CV) risk of the study participants was assessed with WHO non-laboratory, WHO laboratory, and AHA risk assessment tools. The WHO non-laboratory risk assessment classified higher proportion of patients as high risk categories 17.8% (32) followed by AHA 8.3% (15) and WHO laboratory score 2.8% (5). The risk classification proportions are presented in Figure 1.

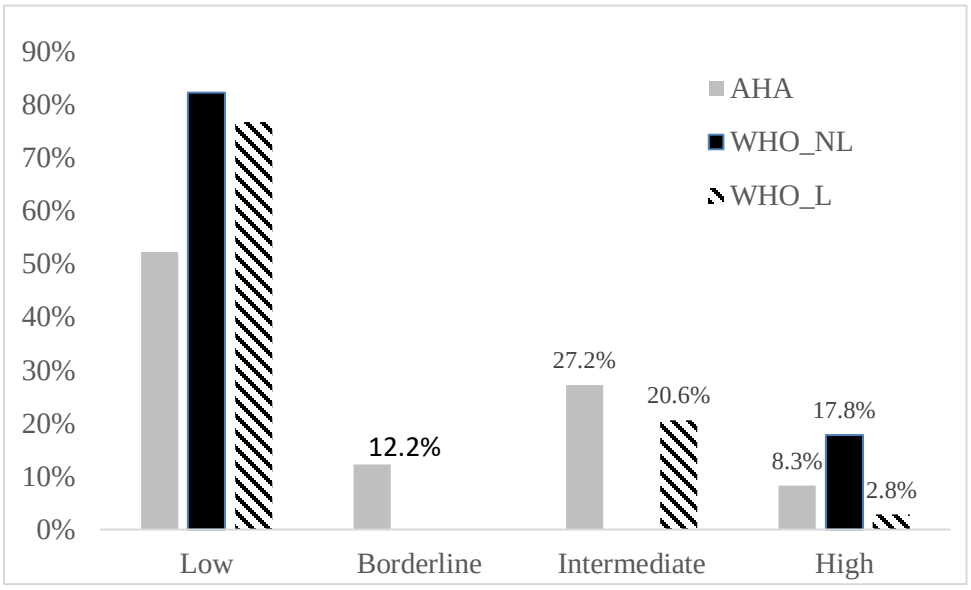
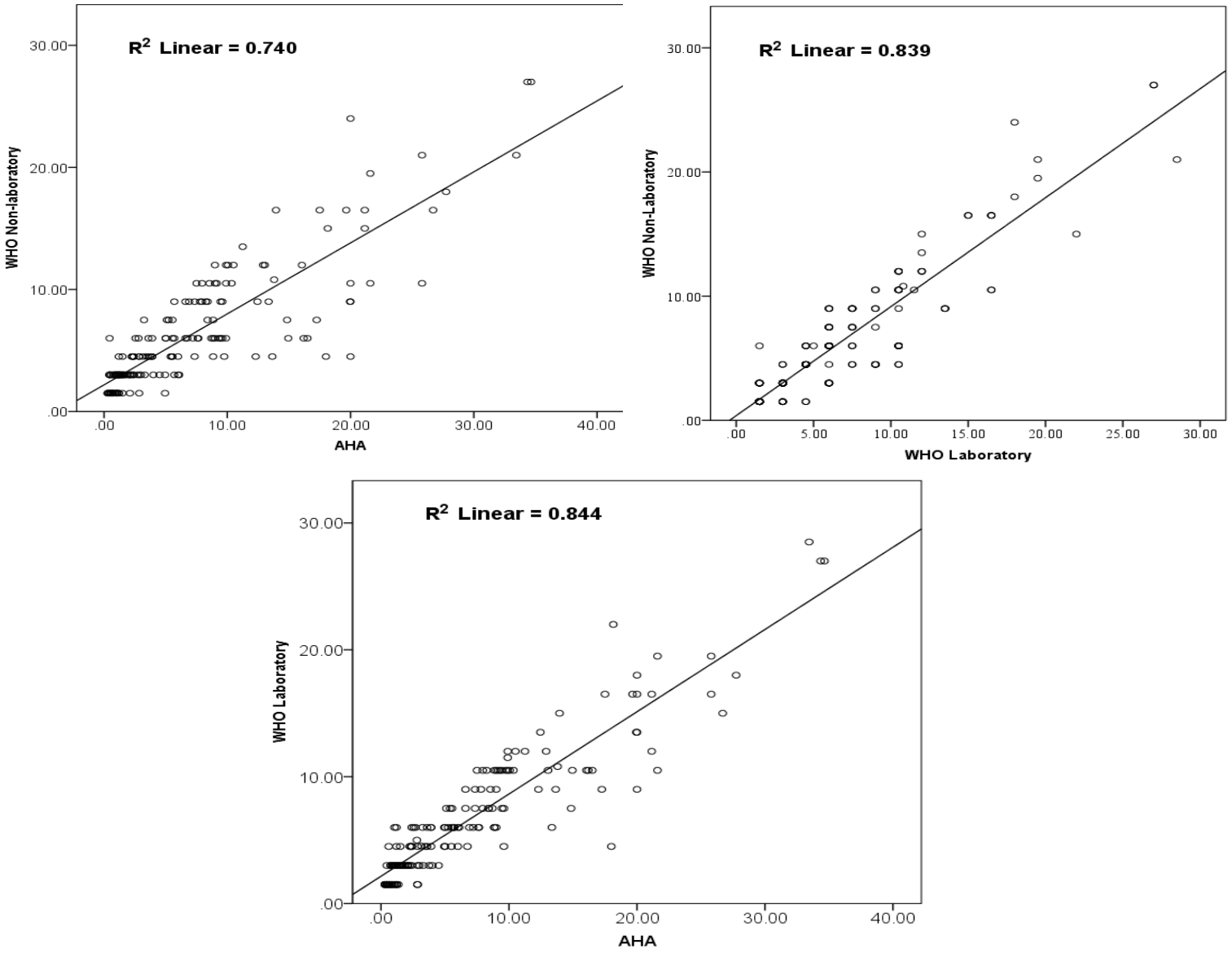


Figure 3: Ten year CV Risk Classification of Study Participants with WHO laboratory, non-laboratory, and AHA risk Assessment Tools

Spearman's rank correlation test was performed to compare the relationship between the three measures of 10-year CV risk (Figure 1). The result showed stronger positive correlation between WHO Laboratory and non-laboratory risk assessment tools: r (178) = .887, p = .000 than WHO-non-laboratory and AHA: r (178) = .863, p = .000. Even though WHO laboratory risk assessment classified only 2.8% of patients as high risk it showed the strongest positive correlation with the AHA risk classification tool: r(178) = .915, p = .000.

Figure 4**:** Scatterplot comparing 10-year cardiovascular risk scores of WHO Non-Laboratory, WHO Laboratory, and AHA risk assessment tools



The Chi-square test was conducted to assess the relationship between Socio-Demographic characteristics, Clinical, and Laboratory parameters and high 10-year CV risk classified with WHO non-laboratory risk assessment tool. Factors with statistically significant relation with high 10-year CV risk were gender (p = .008), age group of 61 to 70 (p = .000), retired occupational status (p = .000), smoking (p = .047), and hypertension (p = .000).

A multivariable binary logistic regression test was conducted to evaluate the association between factors related with the outcome of interest. The logistic regression model was statistically significant ($p < .000$). The goodness of fit of the model was assessed with Hosmer-Lemeshow test (Hosmer & Lemeshow, 2000). The test yielded a Chi-square value of 9.8, which was not statistically significant $p = .134$. The Cox & Snells and Negelkerke pseudo-R squares are .41 and 68% which indicated that the model adequately fit the data.

After controlling for gender, occupation and age, hypertension remained to have statistically significant association with high 10 year ASCVD risk score according to the WHO non-laboratory risk assessment tool: B = 1.865, SE = .694, Wald= 7.226, df = 1, p = .007, OR = 6.4 (95% CI = 1.65 – 25.1). In this model, being diagnosed with Hypertension had a 6.4 times higher odds of having a high 10 year ASCVD risk score.(Table 3)

Similarly, age also remained to have significant association with the outcome variable. It was pointed out that those who were 60 years of age and above, had a higher odds of having a high 10 year ASCVD risk score compared to those below 60 years of age. OR= 63.3 (95% CI= 14.1 – 284.6).

Table 3: Multivariable binary logistic regression of factors related with high 10-yr CV risk classification of study participants

Parameters	B	S.E.	Wald	df	p value	COR	95% C.I.	
							Lower	Upper
Gender (M)	1.18	1.18	0.99	1.00	0.32	3.26	0.32	33.5
Hypertension	1.87	0.70	7.23	1.00	0.007	6.45	1.66	23.13
Age(≥60)	4.12	0.77	29.28	1.00	.000	63.33	14.09	284.57
Job (retired)			3.49	4.00	0.48			
Government Employee	-1.54	1.29	1.42	1.00	0.23	0.21	0.02	2.70
Private Corporations	-1.87	2.03	0.85	1.00	0.36	0.15	0.00	8.28
Self Employed	-1.12	1.27	0.77	1.00	0.38	0.33	0.03	3.93
Unemployed	-1.17	0.71	2.68	1.00	0.10	0.31	0.07	1.26
Constant	-3.85	.94	16.97	1.00	0.00	0.021		

Among patients classified as high risk with the WHO non-laboratory, high and intermediate risk with WHO laboratory, and AHA CV risk assessment tools only 25% (8), 31% (13), and 23.4% (15) of the study participants were on statins.. There was no statistically significant relationship between

WHO non-laboratory CV risk classification and statin treatment in the sample (p = .081) while both WHO laboratory (p = .001) and AHA (p = .000) risk classifications had statistically significant relation with statin use.

Even though only 27.8% (27) of patients with the diagnosis of dyslipidemia were on statin therapy, there was a statistically significant relationship between having dyslipidemia and statin use (p = .000). Similarly, 27.4% (27) of patients diagnosed with hypertension were on statin therapy and statistically significant relation was observed (p = .000).

Table 4: Utilization of Statin therapy among intermediate and high risk RA patients according to WHO Laboratory, Non-laboratory and AHA/PCE Cardio-vascular risk assessment tools

Characteristics		Sample	On Statins	p value¥
WHO Non-laboratory CV Risk Categories				
	Low	147 (82.1)	19 (12.8)	.081
	High	32 (17.9)	8 (25.0)	
WHO Laboratory CV Risk Categories				
	Low	137 (76.5)	14 (10.1)	.001
	High & Intermediate	42 (23.5)	13 (31.0)	
Dyslipidemia*		96 (53.6)	27 (27.8)	.000
AHA				
	Low and Borderline	115 (64.2)	12 (10.3)	.028
	Intermediate and High	64 (35.8)	15 (23.4)	
Hypertension		72 (40.2)	20 (27.4)	.000

Abbreviation: CV – Cardio-vascular,

*Dyslipidemia diagnosis is assessed with past medical history and ATP-III dyslipidemia definition

¥p values are for Pearson's χ^2 test of independence

6. Discussion

Atherosclerotic cardiovascular disease is a major contributing factor for an increased mortality in patients with Rheumatoid Arthritis.(4) This is due to the higher prevalence of traditional CV risk factors and RA specific novel risk factors.(5,6,7))This study is the first of its kind in Ethiopia, which assessed the 10 year ASCVD risk, its associated factors and utilization of statins among high risk patients with Rheumatoid Arthritis. The prevalence of high 10 year ASCVD Risk score was found to be 17.8% based on the WHO non laboratory risk assessment tool whereas AHA/PCE and WHO laboratory risk assessment tool identified 8.4% and 2.8% of RA patients as high risk. Despite these differences in the CV risk scores, our study has demonstrated a significant positive correlation among the three tools, of which the strongest correlation was obtained by WHO laboratory and AHA/PCE with r(178) of .915 followed by .887 for WHO laboratory and non-laboratory and .863 for WHO non Laboratory and AHA/PCE. This finding implicates that High ASCVD risk is common in RA patients in Ethiopia.

Possible explanation for the discrepancies is explained by the different cutoff values used to categorize high risk patients in the respective risk assessment tools (20% for WHO laboratory and AHA PCE, whereas 10% for WHO Non laboratory risk tools). The later cutoff value of 10% for high ASCVD risk score relates effectively with the laboratory risk assessment tools specifically for non-diabetic patients.(48)

The magnitude of high 10 year CV risk score reported by cross-sectional analysis conducted in Mexico and Italy were higher compared to the findings of this study, with an estimate of 23.2% and 39.3% respectively using the AHA pooled cohort Equation.(31, 33) Possible reasons for this discrepancy can be explained by the differences in the socio-demographic and behavioral characteristics, as their population included a higher number of geriatric age groups and higher proportion of patients were smokers compared to our study (9.3% vs 1.7%) which enhanced their CV risk significantly. The AHA/PCE tool is originally developed for the western countries which might contribute for the possible underestimation of the risk score in our study compared to theirs.

With regards to WHO laboratory risk assessment tool in our study, which has identified only 2.8% of the RA patients as high risk, it categorized a higher proportion of the sample into intermediate and low risk (20.6% and 76.7%) which goes along with one study which described a higher chance of underestimated risk score by the use of CV risk calculators especially for those who are categorized

as low and intermediate risk even after the use of the multiplication factors.(1) Lack of RA specific indicators and markers which identifies subclinical atherosclerosis(as it correlates well with the development of future ASCVD) in the risk assessment tools contribute for underestimation of their true risk.(12,26,30)

The WHO non laboratory risk assessment tool was used for analysis as it highly correlated with the other tools and identified a higher proportion of patients as high risk. On the multivariable regression, hypertension and age were found to be the main determinant factors of high 10 year ASCVD risk score. Accordingly after adjusting for other covariates, hypertension remained to have a significant association with high 10 year ASCVD risk score with a p value of .007, and 6.4 fold increased odds of having a high 10 year ASCVD risk score compared to those who don't have Hypertension. Similar findings from the literature have reported the association of an increase in the systolic blood pressure with a higher occurrence of CV events in RA patients.(50)

Our study has also shown that increment in age is a significant predictor of high 10 year ASCVD risk score with a p value of .000. Those with age of 60 and above had higher odds of having an elevated 10 year ASCVD risk score compared to those below 60 years of age. Similar findings were reported in a population based inception cohort study in Minnesota, where aging increased the predicted CVD risk of RA patients exponentially.(49) The same study has also demonstrated that the presence of seropositivity doubled the effect of age on CV risk which is far-fetched to demonstrate in our study because of the study design. (49)and not adequately powered to look into the effect size because of the wide confidence interval produced in our study which can be explained by the relatively smaller sample size.

Our results have demonstrated the magnitude of traditional Cardiovascular risk factors among RA patients among which Dyslipidemia was found to be the commonest one(53.3%) a higher proportion compared to previous studies done in Mexico.(32) Hypertension accounted for 40% of the sample in our study and similar findings were obtained in previous literatures which revealed a prevalence of 57% and 33% in two different studies.(17, 32). Hypertension was found to be the main driver of high 10 year ASCVD risk score as it was prevalent among the study participants. The third common CV risk factor was Diabetes mellitus(16.1%) with similar findings compared to the previous studies in India(12%) and Mexico(13.4%).(30,32) Smoking history (both current and previous) accounted for

1.7% of RA patients in our study which is very low in contrast to studies done in India and Mexico.(31, 32)

Concerning primary prevention measures, only 25% of high risk(WHO non laboratory), 31% of intermediate and high risk groups(WHO laboratory) and 23.2% of intermediate and high risk(AHA/PCE) were on statins in our study which is a very low practice compared to the standard as the American Heart Association and WHO recommend statin therapy for primary prevention for RA patients with intermediate and high 10 year ASCVD risk scores. This result is similar with a study conducted in Mexico where only 14.7% of the high risk groups were taking statins where as another study revealed that 24.8% of the high risk groups were not on statins.(30,31)

7. Conclusion and recommendations

Elevated 10 year ASCVD risk score is common among Rheumatoid Arthritis Patients in Ethiopia. Our study has demonstrated a high ASCVD risk score of 17.6% with the WHO non laboratory risk assessment tool which highly correlates with the AHA/PCE and WHO laboratory CV risk assessment tools. Age and Hypertension are the main drivers for a high 10 year ASCVD risk score. In spite of the broad range of high ASCVD risk score among RA patients, primary prevention measures are poor as only one third of the high risk groups were on statins.

Despite the lack of a universally recommended/accepted risk assessment tool to assess all RA patients, we recommend the use of WHO non laboratory risk assessment tool in our country, Ethiopia, as it is easy and feasible to use and better identifies high risk groups in a setting of limited resources. In addition, statins have to be instituted for all high and intermediate risk groups with Rheumatoid arthritis for primary prevention.

Further prospective observational studies with larger sample size are required to determine which risk score correlates best with the development of ASCVD in 10 years.

8. Limitations of the study

Possible limitations of this study include, the nature of the study design. As it is a cross sectional one, it makes it difficult to estimate the true incidence of Cardiovascular events as an outcome, but it gives an input for future large prospective cohort studies.

The study has also failed to find significant association between high ASCVD risk and Rheumatoid arthritis specific variables which could be explained by the lack of RA specific variables in the CV risk assessment tools.

Subclinical atherosclerosis was not assessed because of budget constraints for imaging modalities (Carotid Doppler U/S to assess Carotid media intima thickness) which strongly correlates with the risk of CV events in the future.

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Annexes

Annex 1: Assurance of the primary investigator

I, the undersigned agree to accept all the responsibilites for the scientific, ethical and technical conduct of the research project. I will provide timely progress report to my advisors and seek the necessary advice and approval in the course of the research. I will communicate timely to my advisors, and all stake holders involved in the study including any source of funding for this research.

Name of the Primary Investigator:

Yemisrach Kifle Shewangizaw (MD, 3rd year IM resident)

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Date_____Signature_____

Approval of my advisors

Advisors Name:

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አባሪ 1፡ የባለ ጥናቱ ማረጋገጫ

ስሜና ፊርማዬ ከዚህ በታች የተመለከተው፤ የምርምር ፕሮጀክቱን ሳይንሳዊ፣ ሙያዊ እና ቴክኒካል ስነ-ምግባር እንዲሁም በምርምር ውሎች እና ሁኔታዎች መሰረት የሚፈለጉትን ወቅታዊ የሂደት ሪፖርቶችን ለማቅረብ ሀላፊነቱን እወስዳለሁ፡፡ በምርምር ሂደቱ ውስጥ አስፈላጊውን ምክር እና ፍቃድ ከአማካሪዎቼ እጠይቃለሁ።

ለአማካሪዎቼ እና በጥናቱ ውስጥ ለሚሳተፉ ለሁሉም ባለድርሻ አካላት ለዚህ ምርምር ማንኛውንም አይነት ሂደትና የገንዘብ ምንጭን ጨምሮ በጊዜው አሳውቃለሁ ።

ስም፡- የምስራች ክፍሌ ሸዋንግዛው (ዶ/ር, 3ተኛ ዓመት የውስጥ ደዌ ህክምና ተማሪ)

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ቀን_____ፊርማ_____

የጥናቱ አማካሪዎች ስም፡-

1. ዶ/ር ብርሃኑ ደመላሽ (የውስጥ ደዌ ስፔሻሊስት እና የመገጣጠሚያና አያያዥ ጡንቻዎች ንዑስ ስፔሻሊስት)

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ቀን _____ፊርማ_____

2. ዶ/ር ደጁማ ያደታ (የውስጥ ደዌ ስፔሻሊስት እና የልብ ንዑስ ስፔሻሊስት)

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ቀን _____ፊርማ_____

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የኢሜል አድራሻ፡ imed.som@aau.edu.et

አዲስ አበባ፣ ኢትዮጵያ

Annex 2: Participant information sheet

Good morning/afternoon dear participant! My name is _____. I am working as a data collector for the study being conducted to assess the 10 year cardiovascular risk & prevention strategies among patients with Rheumatoid Arthritis done by Dr Yemisrach Kifle Shewangizaw (3rd year internal medicine resident). Please allow me to take a moment to explain the study and how you were chosen to participate in it. If something is unclear, don't hesitate to ask, and take your time in determining whether or not you choose to participate in this study. I want to underline that participation in the study is completely voluntary. You will not be penalized if you choose not to participate in this study or if you decide to stop participating at any point.

It is well known that ASCVD is the main cause of death in patients with Rheumatoid Arthritis, due to the higher prevalence of traditional risk factors and other novel risk factors. This has been shown in the literature and the guidelines recommend a routine CV screening for all RA patients. Despite this, there is no formal CV risk assessment practice in our RA patients and datas are lacking in Ethiopia and Africa regarding CV risk in these particular patients, which raised this research question.

The objectives of this study are to assess the 10 year atherosclerotic cardiovascular risk, to identify CV risk factors and assess CV risk management in patients with Rheumatoid Arthritis.

The study will run from September 1 through November 30, 2023, G.C. Through the use of structured questionnaires, data will be gathered. Should you consent to participate in this research, you will be required to fill out the accompanying questionnaire.

All the required physical examination measurements and biochemical study results which are done in the past 3 months will be taken for the purpose of the study.

Every piece of information collected for the study will be kept private. Your name will not appear in presentations of the study's findings made at meetings or in papers published in a journal.

There will be neither incentives, nor direct benefit for you for participating in this study. However, the results from the study may give input to primary care physicians, Internists and Rheumatologists in maximizing care for patients with Rheumatoid arthritis. There are no medical

risks to you from participating in this study

You can consult the contact person listed below, if you have any questions about the study before/during your involvement.

Yemisrach Kifle (MD, 3rd year IM resident)
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E-mail address: yemkifle2@gmail.com

ውድ ተሳታፊ! ስሜ_____ይባላል። በዶ/ር የምስራች ክፍሌ ሸዋንግዛው (የ3ኛ አመት የውስጥ ደዌ ስፔሻላይዜሽን ተማሪ) በቀረበው በሩማቶይድ አርትራይተስ ባለባቸው ታማሚዎች ላይ በ 10 አመት ውስጥ ሊከሰት ስለሚችል የልብ ህመም; ስጋት እና መከላከያ ዘዴዎችን ለመገምገም እየተካሄደ ላለው ጥናት መረጃ ሰብሳቢ ሆኜ እየሰራሁ ነው።

ስለ ጥናቱ እና ለጥናቱ ተሳታፊነት በመመረጥዎ ያሉትን መረጃዎች አሳውቆት ዘንድ ትኩረት እንዲሰጡኝ በአክብሮት እጠይቃለሁ።

ከ40 አመት በላይ በመሆንዎ እና ከሩማቶይድ አርትራይተስ ህመም ጋር የሚኖሩ ስለሆኑ በዚህ ጥናት ላይ እንዲሳተፉ ተጋብዘዋል። በዚህ ጥናት ውስጥ 199 ግለሰቦች ይሳተፋሉ:: በጥናቱ ላይ ለመሳተፍ ከመወሰንዎ በፊት ጥናቱ ለምን እንደሚደረግ እና ምን እንደሚያካትት መረዳት ለእርስዎ አስፈላጊ ነው። እባክዎ የሚከተለውን መረጃ በጥንቃቄ በማንበብ፤ ግልጽ ካልሆነ ለመጠየቅ ወይም ከሚፈልጉት ሰው ጋር ለመወያየት በቂ ጊዜ ይውሰዱ።

በዚህ ጥናት ውስጥ መሳተፍ ሙሉ በሙሉ በፈቃደኝነት ላይ የተመሰረተ መሆኑን ልናሳስብ እንወዳለን፣ በዚህ ጥናት ላይ አለመሳተፍ ወይም በማንኛውም ጊዜ ተሳትፎዎን ማቋረጥ ይችላሉ። ይህ በእርሶ ላይ የሚያመጣው ምንም አይነት ችግር አይኖርም::

ሩማቶይድ አርትራይተስ ባለባቸው ታማሚዎች ላይ ለሞት የሚዳርግ ዋነኛ መንስኤ የልብና ተያያዥ የደምስር በሽታ(ASCVD) መሆኑ ይታወቃል:: ይህም ከጤናማ ሰዎች ጋር ሲነጻጸሩ በልብና ተያያዥ የደምስር በሽታ(ASCVD) ህመም የመያዝ እድላቸው የሰፋ በመሆኑ በሽታው(ሩማቶይድ አርትራይተስ) እንደ አንድ ዋነኛ አጋላጭ ምክንያት ተደርጎ ይያዛል። ከእድሜና አካባቢያዊ ለውጥ ጋር ተያይዘው የሚመጡ አጋላጭ መንስኤዎችን ጨምሮ ከሩማቶይድ አርትራይተስ (RA) ጋር ብቻ የተያያዙ ምክንያቶች የልብና ደምስር ህመም በRA ታማሚዎች ላይ ተጋላጭነታቸውን ለመጨመር ዋነኛ ምክንያቶች ናቸው። ይህም በተለያዩ ስነ-ጽሑፎች ውስጥ ተገልጿል:: የሩማቶይድ አርትራይተስ መመሪያዎችም ለሁሉም የ RA ታካሚዎች መደበኛ የCV(የልብና ተያያዥ) ምርመራ እንዲደርግ ይመክራሉ። ይህም ሆኖ ግን በ RA ታካሚዎቻችን ላይ ምንም ዓይነት መደበኛ የCV(የልብና ተያያዥ ህመም እና አጋላጭ) ምርመራ ልምድ የለም።

በኢትዮጵያ፣ በአፍሪካ እና በሌሎች ዝቅተኛ እና መካከለኛ ገቢ ባላቸው አገሮች ውስጥም እንዲሁ RA በሽታ ላለባቸው ታካሚዎች የልብና ደምስር ህመም በሽታዎች ስፋት መጠን እና አጋላጭ ምክንያቶች ላይ የመረጃ እጥረት አለ። እነዚህ ምልከታዎች እና የችግሩ መጠን ስፋት ያልታወቀ በመሆኑ በእኛ መዋቅር ውስጥ እነዚህን የምርምር ጥያቄዎች አስነስቷል።

የጥናቱ ዓላማዎች RA ባለባቸው ታካሚዎች ላይ የ 10 አመት የልብናተያያዥ የደም ሥር ህመም ስጋትን (cardiovascular risk) ለመገምገም, የCV (የልብ ህመም) አጋላጭ ሁኔታዎችን ለመለየት እና ከፍተኛ አጋላጭ ሁኔታዎች ላሏቸው ታካሚዎች (high CV disease risk) መከላከያ መንገዶችን መገምገም ነው።

ይህ ጥናት እ.አ.አ. ከሰኔ 1 ቀን እስከ ነሐሴ 30 ቀን 2023 በመረጃ መጠይቆች ይሰበሰባል። ጥናቱ ላይ ለመሳተፍ ፍቃደኛ ከሆኑ ለመጠይቁ መልስ እንዲሰጡ ይጠበቅብዎታል።
አካላዊ ምርመራዎችን ጨምሮ ባለፉት 3 ወራት ውስጥ የተሰሩ የላብራቶሪ ውጤቶች ለጥናቱ አላማ ሲባል ይሰበሰባሉ።

በጥናቱ የተሰበሰቡ ሁሉም መረጃዎች በሚስጥር ይያዛሉ። የጥናቱ ውጤት በስብሰባዎች እና በ ሳይንሳዊ መጽሔት ውስጥ በሚታተሙበት ጊዜ የተሳታፊውን ስም አይጨምሩም።
በዚህ ጥናት ውስጥ ለመሳተፍ ምንም አይነት ክፍያ አይኖርም። በመሳተፎትም የሚደርስበት አደጋ ወይንም ስጋት አይኖርም።
ስለ ጥናቱ ማንኛውንም አይነት ጥያቄ ካለዎት ከዚህ በታች የተመለከተውን ሰው ማማከር ይችላሉ።

የምስራች ክፍሌ (MD, 3rd year IM resident)

ስልክ፡ +251 922 961 242

ኢሜል አድራሻ፡ yemkifle2@gmail.com

Annex 3: Declaration of informed voluntary consent

The participant information sheet has been read to me. I have a good understanding of the study's objectives, methods, advantages and disadvantages, confidentiality concerns, participation rights, and address for any questions. I have the option to ask questions about anything that's not quite clear. I was told that I may opt out of the study at any moment and that I was not required to respond to any questions. Consequently, I hereby voluntarily consent to be a participant in this study and sign my name with my initials as shown below.

Contact Address: Phone number:_____

E-mail address:_____

Signature of participant _____

Name of Data collector _____Signature of Data collector_____

አባሪ 3፡ የፈቃደኝነት ስምምነት ምስክር ወረቀት

ከላይ ያለውን የተሳታፊውን የመረጃ ወረቀት በሚገባ አንብቤያለሁ። የጥናቱ ዓላማ፣ አካሄዶች፣ ስጋቶች እና ጥቅሞች፣ ሚስጥራዊነት፣ የመሳተፍ መብቶች እና ለማንኛውም መጠይቆች የባለ ጥናቱ አድራሻ በግልፅ ተነግሮኝ ተረድቻለሁ። ግልጽ ባልሆኑ ጉዳዮች ላይ ጥያቄዎችን እንድጠይቅ እድል ተሰጥቶኛል። በማንኛውም ጊዜ ከጥናቱ የመውጣት ወይም የማልፈልገውን ማንኛውንም ጥያቄ ላለመመለስ መብት እንዳለኝ ተነግሮኛል። ስለዚህ ከዚህ በታች እንደተገለጸው በዚህ ጥናት ላይ ለመሳተፍ በፈቃደኝነት መስማማቴን በፊርማዬ አረጋግጣለሁ።

የተሳታፊ አድራሻ፡ ስልክ ቁጥር_____

ኢሜል አድራሻ፡ _____

የመረጃ ሰብሳቢው ስም _____

የመረጃ ሰብሳቢው ፊርማ _____

Annex 4: Standard Questionnaire

Eligibility Assessment		**Response**	
		Yes	**No**
Established ASCVDs	Coronary Heart Disease		
	Cerebrovascular Disease		
	Peripheral arterial Disease		
	Aortic disease		
Severe Illness/critically ill			
Age less than 40 years old			
If response to any one of the above questions is **Yes, End**			
Consent has been read and obtained		**If No,** END	

Interview Language and Code	**Response**
Interview Language *[Insert Language]*	
MRN/ I - care number/Code	
Contact phone number	

Step 1: Questionnaire on Sociodemographic Information

Question	**Response**			
Sex	Male 1	Female 2		
Age	Years _____			
Level of education	No formal schooling 1	High school completed 5		
	Less than primary school 2	College/University completed 6		
	Primary school completed 3	Post graduate degree 7		
	Secondary school completed 4			
Region	Tigray 1	Somali 5	Gambella 9	
	Afar 2	Benishangul-Gumuz 6	Addis Ababa 10	
	Amhara 3	SNNPR 7	Dire-Dawa 11	
	Oromia 4	Harari 8		
Marital status	Never married 1	Divorced 4		
	Currently married 2	Widowed 5		
	Separated 3			
Current Job	Government employee 1	Non-paid 4	Retired 7	
	Non-government employee 2	Student 5	Unemployed (able to work) 8	
	Self-employed 3	Homemaker 6	Unemployed (unable to work) 9	
Monthly income	<5000ETB 1	5,000-10,000ETB 2	10,000-20,0000ETB 3	>20,000ETB 4

Step 1: Questionnaire: Behavioral & Clinical Assessments

Question	**Response**	
Current smoking	Yes 1	No 2
Previous smoking	Yes 1	No 2
If yes to smoking	Number of years_____	Number of cigarettes/day_____
Alcohol intake history	Yes 1 No 2	
If yes, to Alcohol intake	Amount (in local measurements)_____ _____ Frequency per week_____, Total duration of intake____	
Exercise Habit	Yes 1 Frequency per week_____ Duration per day _____(in minutes) Type of exercise _____	
	No 2	
Hypertension	Yes 1, Duration _____	
	No 2	
Treatment for hypertension	Yes 1 Medications _____ ____	
	No 2	
Diabetes or Pre-diabetes (IFG, IGT)	Yes 1, Duration _____	
	No 2	
Treatment for Diabetes	Yes 1, Medications_____	
	No 2	
Dyslipidemia (Abnormal Cholesterol)	Yes 1, Duration _____	
	No 2	
Treatment for Dyslipidemia	Yes 1, Statin type _____, dose_____ Other agents _____(if any)	
	No 2	

RA disease duration		
RA disease activity		
Extra articular manifestations		
DMARDs use	Methotrexate 1	Biological DMARDs
Corticosteroid use	Yes 1 If yes, dose_____ _____	No 2
NSAIDs use	Yes 1	No 2

Step 2: Physical Measurements

Question	**Response**
Blood Pressure	Systolic (mmHg)_____Diastolic (mmHg)_____
Height	in Centimetres (cm) _____
Weight	in Kilograms (kg)_____
Calculated BMI	In kg/m^2 _____

Step 3: Biochemical Measurements

Question		**Response**
FBS/Hgb A1C		_____/_____
Lipid profile	LDLc	_____
	HDLc	_____
	Total cholesterol	_____
	Triglyceride	_____
RF		_____
Anti CCP		_____
CRP		_____

Thank you for your time!

አባሪ 4፡ መደበኛ መጠይቅ

ለጥናቱ ተሳታፊነት ብቃት ግምገማ		**ምላሽ**	
		አዎ	**አይ**
ASCVDs የልብ ህመም	የልብ ህመም		
	ስትሮክ ህመም		
	የደም ስር ህመም		
	የአኦርቲክ(የትልቁ ደም ቧንቧ)በሽታ		
ከባድ ሕመም			
ዕድሜ ከ 40 ዓመት በታች			
ከላይ ከተዘረዘሩት ጥያቄዎች ውስጥ ለአንዱ ምላሽ አዎ ከሆነ፣ ጨርስ			
ፈቃድ ተነቧል እና ተፈርሟል		**አይ ከሆነ፣ ጨርስ**	
የቃለ መጠይቅ ቁንቁ እና ኮድ		**ምላሽ**	
የቃለ መጠይቅ ቁንቁ [ቁንቁ አስገባ]			
MRN / I -care ቁጥር / ኮድ			
የተሳታፊ ስልክ ቁጥር			

ደረጃ 1፡ በሶሺዮዲሞግራፊ መረጃ ላይ መጠይቅ

ጥያቄ	**ምላሽ**		
ፆታ	ወንድ 1	ሴት 2	
ዕድሜ	ዓመታት _____		
የትምህርት ደረጃ	ምንም መደበኛ ትምህርት የለም 1	ሁለተኛ ደረጃ ትምህርት ቤት ያጠናቀቀ5	
	ከአንደኛ ደረጃ ትምህርት ያነሰ 2	ኮሌጅ/ዩኒቨርስቲ ያጠናቀቀ 6	
	የመጀመሪያ ደረጃ ትምህርት ቤት ያጠናቀቀ3	የድህረ ምረቃ ዲግሪ 7	
	ሁለተኛ ደረጃ ትምህርት ቤት ያጠናቀቀ 4		
ክልል	ትግራይ 1	ሶማሌ 5	ጋምቤላ 9
	አፋር 2	ቤንሻንጉል-ጉሙዝ 6	አዲስ አበባ 10
	አማራ 3	ደቡብ ክልል 7	ድሬዳዋ 11
	ኦሮሚያ 4	ሀረሪ 8	
የትዳር ሁኔታ	ያላገባ 1	የተፋታ 4	
	ያገባ 2	በሞት የተለየ 5	
	የተለያየ 3		
የስራ ሁኔታ	የመንግስት ሰራተኛ 1	ነጻ አገልግሎት 4	ጡረተኛ 7
	የመንግስት ያልሆነ ሰራተኛ 2	ተማሪ 5	ስራ የሌለው (መስራት የሚችል) 8
	በግል ስራ የሚተዳደር 3	የቤት እመቤት 6	ስራ የሌለው (መስራት የማይችል) 9

ወርሃዊ ገቢ	<5000 ብር 1	5,000-10,000ብር 2	10,000-20,0000ብር 3	>20,000ብር 4

ደረጃ 1፡ መጠይቅ፡ የባህሪ እና ክሊኒካዊ ግምገማዎች

ጥያቄ	**ምላሽ**	
አሁን ላይ ሲጋራ ያጨሳሉ	አዎ 1	አይ 2
ከዚህ ቀደም አጭሰው ያውቃሉ	አዎ 1	አይ 2
ምላሹ አዎ ከሆነ	የዓመታት ብዛት_____	የሲጋራ ብዛት/ቀን _____
የአልኮል መጠጥ ይጠቀማሉ	አዎ 1 አይ 2	
ምላሹ አዎ ከሆነ፣	መጠን (በአካባቢው ልኬቶች)____በሳምንት ምን ያህል ጊዜ _____	
የአካል ብቃት እንቅስቃሴ ልምድ	አዎ 1 በሳምንት ምን ያህል ጊዜ _____ በቀን _____(በደቂቃዎች) የአካል ብቃት እንቅስቃሴ አይነት _____	
	አይ 2	
የደም ግፊት	አዎ 1, ምን ያህል ጊዜ _____	
	አይ 2	
ለደም ግፊት ሕክምና	አዎ 1 የመድሃኒት አይነት _____	
	አይ 2	
የስኪር በሽታ ወይም ቅድመ- ስኪር በሽታ (IFG, IGT)	አዎ 1, _ምን ያህል ጊዜ _____	
	አይ 2	
ለስኪር በሽታ ሕክምና	አዎ 1 የመድሃኒት አይነት _____	
	አይ 2	
ዲስሊፒዲሚያ (ከፍተኛ የኮሌስትሮል መጠን)	አዎ 1, _ምን ያህል ጊዜ _____	
	አይ 2	

ለዲስሊፒዲሚያ(ከፍተኛ የኮሌስትሮል መጠን) ሕክምና	አዎ 1, የመድሃኒትዓይነት _____፣ መጠን_____ሌሎች (ካለ)___
	አይ 2

የ RA በሽታ ከታወቀ ምን ያህል ጊዜ ሆነ		
የ RA በሽታ disease activity		
ከመገጣጠሚያ ውጪ ያሉ የRA ምልክቶች		
በ DMARDs ህክምና	Methotrexate 1	Biological DMARDs
በ ኮርቲኮስቴሮይድ ህክምና	አዎ 1 አዎ ከሆነ፣ ልክ መጠን_____	አይ 2
በ NSAIDs ህክምና	አዎ 1	አይ 2

ደረጃ 2፡ አካላዊ መለኪያዎች

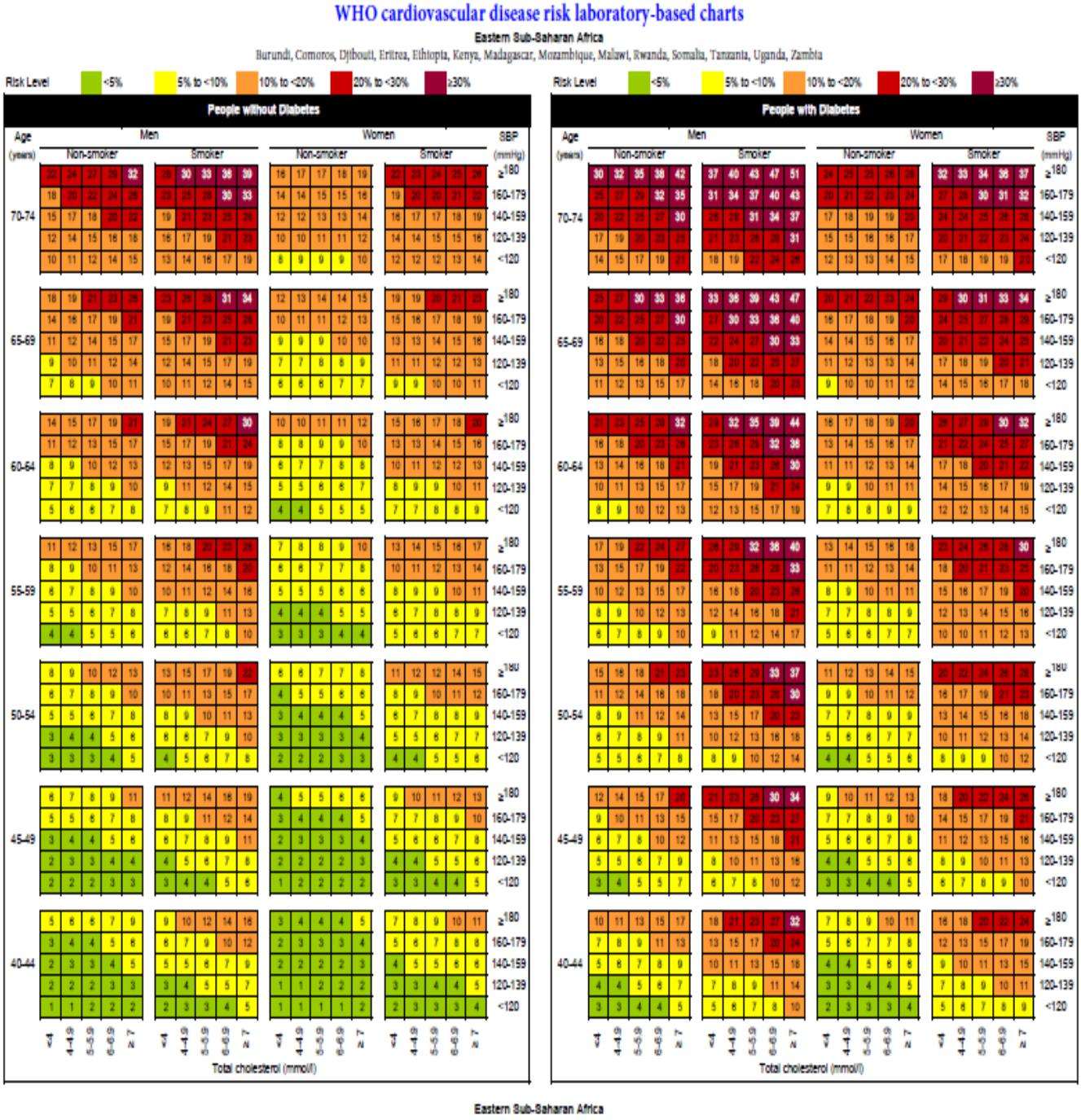
ጥያቄ	**ምላሽ**
የደም ግፊት	ሲስቶሊክ (mmHg)_____ዲያስቶሊክ (mmHg) _____
ቁመት	በሴንቲሜትር (ሴሜ)
ክብደት	በኪሎግራም (ኪግ) _____
የተሰላ BMI	በኪግ/ሜ2 _____ _____

ደረጃ 3: የላብራቶሪ ምርመራዎች

ጥያቄ		**ምላሽ**
FBS/Hgb A1C(የስኳር መጠን)		_____/_____
Lipid profile (ኮሌስትሮል መጠን)	LDLc(ኤልዲኤል ኮሌስትሮል)	_____
	HDLc(ኤችዲኤል ኮሌስትሮል)	_____
	Total cholesterol(ጠቅላላ ኮሌስትሮል መጠን)	_____
	Triglyceride(ትራይግላይሰራይ ድመጠን)	_____
RF		_____
Anti CCP		_____
CRP		_____

ጊዜዎን ስለሰጡኝ አመሰግናለሁ።

Annex 5: WHO Laboratory based CV risk chart



Annex 6: WHO Non-laboratory based CV risk chart