ADDIS ABABA UNIVERSITY

FACULTY OF MEDICINE

DEPARTMENT OF INTERNAL MEDICINE

THE MAGNITUDE OF PREMATURE CORONARY ARTERY DISEASE AND ITS ASSOCIATED FACTORS AMONG PATIENTS WHO UNDERWENT CORONARY ANGIOGRAPHY AT TIKUR ANBESSA SPECIALIZED HOSPITAL, ADDIS ABABA, ETHIOPIA

BY

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A THESIS SUBMITTED TO THE DEPARTMENT OF INTERNAL MEDICINE, FACULTY OF MEDICINE, ADDIS ABABA UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR A SUBSPECIALTY CERTIFICATE PROGRAM IN ADULT CARDIOLOGY.

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The full title of the project:	The magnitude of premature coronary artery disease and its associated factors among patients who underwent coronary angiography at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.
Duration of research	June 2023 -December 2023
Study area	Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia.
Total cost	51,700 Ethiopian birrs

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Abbreviations

ACS-acute coronary syndrome

CAD-Coronary Artery Disease

CCS-Chronic coronary syndrome

CKD-chronic kidney disease

CVD-cardiovascular disease

ECG-Electrocardiography

FBS-fasting blood sugar

HDL- High-Density Lipoprotein

IHD-Ischemic Heart Disease

LAD- Left Anterior Descending

LCX- Left Circumflex

LDL-Low Density Lipoprotein

LVEF- left ventricular ejection fraction

LVH- left ventricular hypertrophy

PCAD-Premature Coronary Artery Disease

PCI- Percutaneous Coronary Intervention

PDA-Peripheral Arterial Disease

RCA-Right Coronary Artery

TASH- Tikur Anbessa Specialized Hospital

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Abstract

Background: Coronary artery disease is a major cause of morbidity and mortality in developing countries with occurrence at a young age and association with diverse cardiovascular risk factors.

Objective: The objective of this study was to assess the magnitude of premature coronary artery disease and its associated factors among patients who underwent coronary angiography at Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia.

Method: A retrospective cross-sectional study was conducted at TASH, Addis Ababa, Ethiopia, on 218 patients who underwent coronary angiography between May 2017 and June 2023. Data on patients' sociodemographic characteristics, cardiovascular disease risk factors, metabolic profile, cardiac imaging, and angiographic findings was collected using a structured data abstraction checklist from patient medical records. Descriptive statistics and logistic regression were used to assess the association between dependent and independent variables using SPSS version 25. An adjusted odds ratio with a 95% confidence interval was used to show the strength of the association, while a p-value<0.05 was used to declare the significance of the association.

Result: A total of 218 patients' medical records were analyzed and revealed a median age of 55 years with male predominance (82.1%). Forty (18.3%) of patients were diagnosed to have premature coronary artery disease (CAD) among a hundred fifty-eight (72.5 %) patients who had angiographically confirmed CAD. Male sex (AOR=3.5, 95%CI: 1.492,8.367), hypertension (AOR=2.8, 95% CI: 1.162,6.767), low HDL (AOR=2.3, 95% CI:1.025,5.191) and admission diagnosis of chronic coronary syndrome (AOR=2.2, 95% CI: 1.035,4.762) were significantly associated with premature CAD.

Conclusion: The magnitude of premature coronary artery disease at TASH is high. It is significantly associated with male sex, hypertension, low HDL, and admission diagnosis of chronic coronary syndrome. Tremendous effort should be applied to preventing, early detection, and control of hypertension and Low HDL at the community and individual level.

Keywords: premature coronary artery disease, coronary angiography**,** magnitude.

Introduction

Background

The ischemic heart disease (IHD) burden and IHD-related deaths in developing regions not only increased faster and exceeded that in developed regions but also affected relatively younger populations and caused premature death between 30–70 years (1).

The insufficient control of metabolic risk factors and epidemiologic transition have become the leading drivers of the IHD burden and IHD-related deaths shifting from developed countries to developing epidemiological (2).

African patients presenting to hospital with acute coronary syndrome were significantly younger than those from the rest of the world (52 ± 12 years vs. 57 ± 12 years, respectively), and had higher levels of hypertension, diabetes, smoking, and depression(3)

There has been a surge in the burden of non-communicable diseases in sub-Saharan Africa (SSA)over the past two decades, driven by increasing incidence of cardiovascular risk factors like unhealthy diets, reduced physical activity, hypertension, obesity, diabetes, dyslipidemia, and air pollution(4).

Compared to economically developed countries, the prevalence of coronary artery disease (CAD) and related complications is relatively low in most regions in Africa and there are variations in reported prevalence rates within the different regions, although there is an upward trend in all the regions of sub-Saharan Africa(5).

The true burden of traditional modifiable atherothrombotic CVD risk factors and their ensuing complications in SSA remains uncertain as most countries are either void of data or have deficient data collection systems that are not sufficiently reliable to enable the counting of appropriate health-system response(6).

Cardiovascular diseases tend to occur at younger ages approximately two decades earlier in SSA populations compared to high-income countries and CVD deaths in sub-Saharan Africa occur at younger ages on average than in the rest of the world(6, 7).

In the INTERHEART Africa study, the major risk factors for IHD in sub-Saharan Africa were hypertension, smoking, diabetes, abdominal obesity, and dyslipidemia which contributed to a population-attributable risk of nearly 90% for acute myocardial infarction. (8)

Statement of the problem

Premature coronary artery disease(PCAD) is a chronic and aggressive disease, with a high rate of ischemic recurrences, a rapid evolution toward multivessel disease and mortality. (9)

Coronary artery disease in young adults has a poor long-term prognosis and leads to devastating outcomes for patients, their families, and has a significant impact on public health. Ethnicity and chronic inflammation, along with traditional modifiable risk factors including smoking and new-onset diabetes appear to be important factors of poor outcomes (10)

There is no universal definition of premature CAD. Most studies have used an age cutoff of 45 or 55 years, whereas older studies used 65 years. The incidence of premature coronary events among all patients with acute myocardial infarction (AMI) depends on the cutoff age. It has been reported that 4%-10% of AMIs occur before the age of 45 years, while the incidence declines if the age limit is lower(11).

Younger patients with coronary artery disease have different cardiovascular risk profiles like being male, history of smoking, family history of coronary artery disease, and dyslipidemia as compared to older patients who are female, hypertensive, and diabetic(12).

Although community-based evidence on the national burden of cardiovascular diseases (CVDs) in Ethiopia is limited, the Global Burden of Disease (GBD) 2017 study data indicated that CVDs are the leading cause of mortality(13).

Coronary artery disease accounted for nearly 50%(44/92) of the cause of sudden death in a study performed on necropsies of the Medico-legal Department of Menelik II Hospital, in Addis Ababa, Ethiopia during the years 1998 and 1999 (14).

In retrospective studies done to assess the treatment outcome of acute coronary syndrome (ACS) patients admitted at different tertiary hospitals in Ethiopia the in-hospital mortality was 24.5%-27.4%. There was male predominance and hypertension was the most frequent risk factor(15-17).

A prospective cohort study carried out on a total of 181 ACS patients admitted to tertiary care hospital in Ethiopia from March 15 to November 15, 2018, showed that the 30-day all-cause mortality rate was 25.4% and Dyslipidemia (48%) and hypertension (44%) were the most common risk factors identified(18)

A retrospective coronary angiographic study conducted at Addis Cardiac Hospital, Addis Ababa, Ethiopia indicated that the median age of patients with coronary artery disease was 56 years and 50 to 59 years was the most frequently affected age range. Hypertension and dyslipidemia were the two most frequent risk factors encountered and the majority of cases had at least one standard risk factor. Smoking was the least frequent risk factor identified among patients suspected to have IHD (19).

Although coronary artery disease occurs relatively at a younger age in Ethiopia as compared to other settings, the exact prevalence of premature coronary artery disease and its associated risk factors was not known. This study was designed to assess the magnitude of premature coronary artery disease and identify associated risk factors.

Justification of the study

Coronary artery disease (CAD) that manifests at a younger age and its risk of recurrence can have devastating consequences for an individual, the family, and the public at large. Prevention of CVDs long before their onset will be more cost-effective than providing interventions at a stage when the disease is well-established and complicated.

Knowing the magnitude and identification of particular risk factors associated with premature coronary artery disease will help to apply preventive measures early. Although cigarette smoking is not common in Ethiopia as compared to others, coronary artery disease in young is not uncommon.

Data regarding the prevalence and cardiovascular risk factors of premature coronary artery disease in Ethiopia is scarce. This project will be a baseline study for subsequent prospective research. The result of this study will help policymakers to know the magnitude of the problem and plan specific primordial prevention at the community level.

Literature review

Definition and Magnitude of Premature CAD

Premature CAD, defined as the occurrence of symptomatic obstructive coronary atherothrombotic lesions before age 45 years, is an aggressive disease despite the currently recommended prevention measures, with high rates of recurrent events and mortality (9).

It is estimated that about 4–10 % of individuals with documented CAD are less than 45 years old. Premature coronary artery disease (PCAD) seems to increase, particularly in developing countries. Clinical studies have affirmed that patients with PCAD have a different clinical presentation, associated CAD risk factors, and coronary angiographic profile compared with the Mature CAD(20)

The prevalence of premature CAD varies and depends on the study population and age cut point used to define it. For instance, the prevalence of premature CAD in Malaysia was 55 %, when age <55 in males and age <65 in females was used and was 16% in males <45 years and females <55 years old_while it was 31 % in the Iraq study. The prevalence of angiographically proven premature CAD (<=45 years) from the epidemiological data in Spain was 9% (21-23).

According to the INTERHEART study, the median age for the first presentation of CAD in Africa was 54 years, South Asian population was 53-year-old whereas, in Western Europe, China, and Hong Kong it was 63-year-old, with also more men than women affected(24).

Abnormal lipids, smoking, hypertension, diabetes, abdominal obesity, psychosocial factors, low consumption of fruits, vegetables, and alcohol, and inadequate regular physical activity account for most of the risk of myocardial infarction worldwide in both sexes and at all ages in all regions(24)

Factors associated with premature CAD

Premature coronary artery disease affects predominantly the male sex and shows a high prevalence of cardiovascular risk factors, mainly tobacco, hyperlipidemia, and a family history of ischemic heart disease. In addition, it is characterized by less extensive coronary atherosclerosis, mainly with the higher presence of single-vessel disease in contrast to older patients, as well as lower initial mortality(22).

The risk factors for PCAD show regional variations, in general, young patients with acute myocardial infarction with obstructive coronary artery disease have a higher prevalence of smoking, lipid disorders, and family history of premature coronary artery disease, and a lower prevalence of diabetes mellitus and hypertension(11).

Conventional risk factors including family history continue to play a pivotal role in premature CAD in Indians. Women have more metabolic risk factors, present at a later age, and have non-ST elevation ACS more often(25).In young smokers in India, the presence of hypertension, central obesity, diabetes mellitus, and metabolic syndrome identifies a subset at increased risk for future acute CAD (26)

Diabetes mellitus, family history of CAD, dyslipidemia, smoking, and hypertension were significantly and positively associated with CAD in young adults compared to healthy age and sex-matched population in Iran(27)

Sub-Saharan African Ethnic origin, inflammatory disease, and persistent smoking were the strongest correlates of the first recurrent event in the long-term evolution of premature coronary artery disease study. Previous similar findings have associated this higher risk with more frequent hypertension, diet habits, and unequal access to prevention and health care(9)

In a retrospective observational study done on patients that have undergone percutaneous coronary intervention in Ethiopia, the mean age of the study participants was 58.6 years and male to female ratio was 4.2. Dyslipidemia and left ventricular hypertrophy were associated with the extent of coronary artery disease(28).

The prevalence of smoking in Ethiopia as compared to other countries is low 4.5% in males and 1% in females (29) and family history of cardiovascular disease occurs in only 8.5% of study participants done in eastern Ethiopia although hypertension, dyslipidemia, and physical inactivity were common among diabetic patients (30). The magnitude of PCAD and its peculiar associated risk factors are not addressed in Ethiopia.

Objective

General objective:

- To assess the magnitude of premature coronary artery disease and its associated factors among patients who underwent coronary angiography at TASH, Addis Ababa Ethiopia

Specific objectives:

- To determine the magnitude of premature coronary artery disease among patients who underwent coronary angiography at TASH, Addis Ababa Ethiopia
- To identify associated factors of premature coronary artery disease among patients who underwent coronary angiography at TASH, Addis Ababa Ethiopia

Methodology of the Study

Study design

A retrospective cross-sectional study design with both descriptive and analytic components was applied to clinically diagnosed coronary artery disease patients who underwent coronary angiography at TASH, Addis Ababa Ethiopia between May 2017 and June 2023.

Study area and period

The study was conducted at Tikur Anbessa Specialized Hospital from June 2023 to December 2023**.** Tikur Anbessa Specialized Hospital is one of the oldest and largest university hospitals located in the capital city of Ethiopia, Addis Ababa with different inpatient, outpatient, cardiac catheterization laboratories and critical care services.

Study population

All clinically diagnosed coronary artery disease patients underwent coronary angiography between May 2017 and June 2023 at TASH, Addis Ababa Ethiopia.

Inclusion criteria-

- adults >18 years old clinically diagnosed coronary artery disease patients who underwent coronary angiography between May 2017 and June 2023 at TASH, Addis Ababa Ethiopia

Exclusion criteria-

- patients with a history of previous coronary angiographically confirmed CAD
- patients with coronary angiography done for other indication

Sample size and sampling procedure

The sample size was determined by using the single population proportion formula.

n= (Z α/2) 2 p (1-p)/ d2

Where: -

o n = is the calculated sample size

o Z = Confidence interval [95%]

o p = proportion of premature coronary artery disease (50%) assumption

o d2 = marginal error [5%]

n = ((1.96) 2 x 0.5 [1-0.5])/ (0.05)2 = 384

Since the source population 502 was less than 10,000**, a** correction formula was used to adjust the sample size, accordingly: Nf= n/ (1+n/N) Where: -

o n = is the calculated sample size

o N = is the source population (all clinically diagnosed coronary artery disease patients who underwent coronary angiography)

o Nf = Final sample size

= 384/(1+384/502= 218

The final sample size was **218**

Every other patient starting from serial number one was selected from coronary angiography registration till the final sample size was achieved.

Study variables

Dependent variable -premature coronary artery disease

Independent variable- sociodemographic characteristics (sex, age, address), cardiovascular risk factors (hypertension, diabetes, dyslipidemia, family history of CVD, smoking, obesity, stroke, CKD, PAD), laboratory profile, cardiac imaging findings

Operational definitions

Chronic coronary syndrome -patients labeled as having ischemic heart disease, stable angina

Acute coronary syndrome -patients labeled as unstable angina, ST-elevated myocardial infarction, or non-ST-segment elevation myocardial infarction

Premature coronary artery disease -angiographically confirmed coronary artery disease with age of diagnosis<45 years in males and < 55years in female

Mature coronary artery disease - angiographically confirmed coronary artery disease with age of diagnosis >=45 years in males and >=55years in females

Coronary artery disease- a pathological process characterized by atherosclerotic plaque accumulation in the epicardial arteries, whether obstructive or non-obstructive and confirmed angiographically

Hypertension – Hypertension was defined as office systolic blood pressure (SBP) values >_140 mmHg and/or diastolic BP (DBP) values >_90 mmHg or a history of hypertension or use of antihypertensive agents;

Diabetes –presence of any of the following; fasting plasma glucose level >=126 mg/dL, HgA1c >=6.5 %, random blood glucose level >= 200 mg/dL, or a history of diabetes or patient on antidiabetic medication.

Dyslipidemia- presence of one or more of the following four lipid disorders a low-density lipoprotein >=100 mg/dL, triglyceride level of >= 150 mg/dL, and high-density lipoprotein level < 40 mg/dL, and total cholesterol of >=200 mg/dL or history of dyslipidemia

Family history of CVD-history of cardiovascular disease like stroke, coronary heart disease, or peripheral artery disease in first-degree relatives

Obesity -body mass index of >=30kg/m2

Left ventricular hypertrophy-two-dimensional echocardiographic report of left ventricular hypertrophy based on diastolic wall thickness

Left ventricular ejection fraction – two-dimensional echocardiographic report of left ventricular systolic function in percent

Data collection instrument and procedure

A structured data abstraction checklist was prepared by the principal investigator, pretested, and filled out by a trained data collector**.** Sociodemographic data, cardiovascular risk factors, laboratory profiles, cardiac imaging, and coronary angiography findings were collected from patient medical records and coronary angiography registration.

Data analysis procedure

Data was -entered into the SPSS version 25 package for analysis. Descriptive statistics to assess the frequency of variables and Bivariate logistic regression were used to assess the independent effect of age, gender, family history of CVD, obesity, smoking status, diabetes, dyslipidemia,

chronic kidney disease (CKD), peripheral arterial disease (PAD), stroke, metabolic panel, and echocardiographic findings on premature coronary artery disease as a screening in selection of variables for further analysis.

All variables with P- value less than 0.25 were included in the multivariate logistic regression analysis. The method that was used for variable selection was the backward and forward stepwise procedure. All possible 2-way interactions were checked and those significant variables were included in the model. The independent variables were fitted into multiple logistic regression and multicollinearity was checked. The fitness of the model was tested by the Hosmer Lemeshow Goodness of Fit test, the classification table, and the receiver operator characteristic curve.

Ethical Considerations

The proposal was submitted to the Department of Internal Medicine, Faculty of Medicine, Addis Ababa University, for ethical clearance from the ethical review committee. The proposal got permission to access patients' medical records and a waiver of the requirement for informed consent was granted. The study was conducted after research ethical approval was obtained.

Results

Socio-demographic characteristics and CVD risk factors

A total of 218 adult clinically diagnosed coronary artery disease patients who underwent coronary angiography were included in the study. The mean and median age of patients was 54.8(SD.12.4) and 55 years respectively. Males accounted for 82.1% of cases and nearly two-thirds of patients (66.1%) were from Addis Ababa. Hypertension (54.1%), Diabetes Mellitus (47.2%), and Dyslipidemia (24.8%) were the three most common CVD risk factors identified in patients but only one-fifth (20.6%) and one-tenth (11%) of patients were ever smoker and obese respectively (Table 1).

Table 1. Socio-demographic characteristics and CVD risk factors of patients undergoing coronary angiography at TASH, Addis Ababa, Ethiopia between May 2017 and June 2023 (n-218)

Variable	Category	Frequency	Percent
Sex	Male	179	82.1
	Female	39	17.9
Age	<40	24	11.0
	40-60	126	57.8
	>60	68	31.2
Address	Addis Ababa	144	66.1
	Outside Addis Ababa	74	33.9
Hypertension	Yes	118	54.1
	No	100	45.9
Diabetes Mellitus	Yes	103	47.2

	No	115	52.8
Dyslipidemia	Yes	54	24.8
	No	164	75.2
Obesity	Yes	24	11.0
	No	194	89.0
Ever smoking	Yes	45	20.6
	No	173	79.4
Stroke	Yes	3	1.4
	No	215	98.6
CKD	Yes	17	7.8
	No	201	92.2

CKD-chronic kidney disease

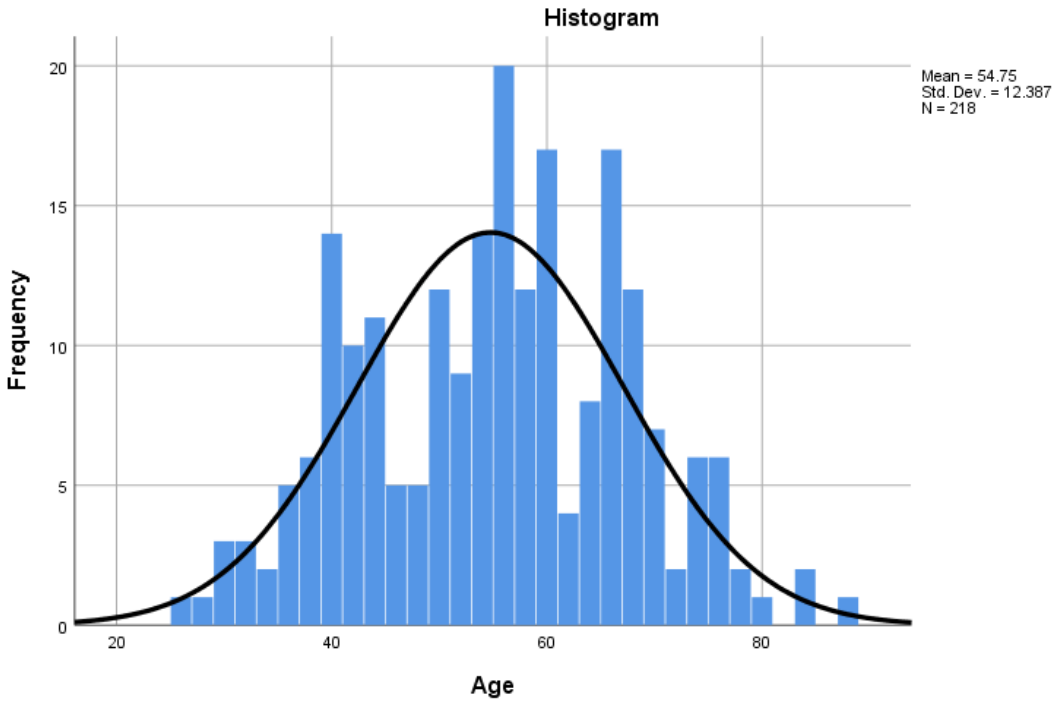

Figure 1- age distribution of patients undergoing coronary angiography at TASH, Addis Ababa, Ethiopia between May 2017 and June 2023 (n-218)

Metabolic profile and echocardiographic findings

More than two-thirds (67.5%) of patients had glycated hemoglobin level >= 5.7 % and more than half (55.5%) of patients had HDL cholesterol <40mg/dl. The mean left ventricular ejection fraction of patients in this study was 47.3 %(SD.13.3). Nearly half (47.7%) of patients had left ventricular ejection fraction (LVEF) >=50% and thirty-five percent of patients had echocardiographic evidence of left ventricular hypertrophy (Table 2).

Table 2. Metabolic profile and echocardiographic findings of patients undergoing coronary angiography at TASH, Addis Ababa, Ethiopia between May 2017 and June 2023 (n-218)

Variable	Category	Frequency	Percent
HgA1c	<5.7	71	32.6
	5.7-6.4	49	22.5
	>=6.5	98	45.0
Total cholesterol	<200	175	80.3
	>=200	43	19.7
LDL-cholesterol	<100	153	70.2
	>=100	65	29.8
HDL-cholesterol	<40	121	55.5
	>=40	97	44.5
Triglyceride	<150	148	67.9
	>=150	70	32.1
LVH	Yes	77	35.3
	No	141	64.7
LVEF	<=40	86	39.4
	41-49	28	12.8
	>=50	104	47.7

LDL-low density lipoprotein-high density lipoprotein, LVH-left ventricular hypertrophy, LVEF-left ventricular ejection fraction

1=LVEF <=40
2=LVEF 41-49
3=LVEF >=50

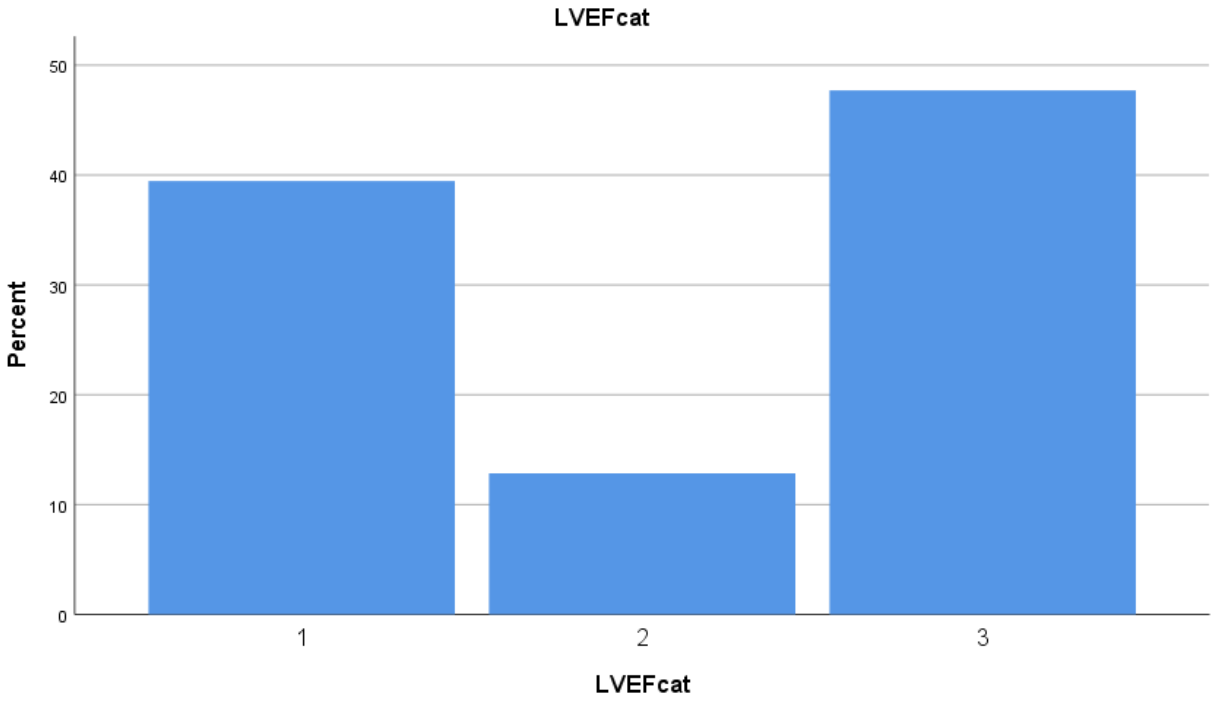

Figure 2-LVEF category of patients undergoing coronary angiography at TASH, Addis Ababa, Ethiopia between May 2017 and June 2023 (n-218)

Diagnosis and coronary angiographic findings

The most common admission diagnosis in this study was chronic coronary syndrome accounting for 56.4%. Coronary artery disease was diagnosed angiographically in 72.5% of patients with nearly one quarter (18.3 %) found to be premature CAD and the remaining 54.1% were mature CAD. While the left anterior descending (LAD) coronary artery was diseased in 61% of patients followed by the right coronary artery (RCA) in 27.1% of patients, the left main coronary artery was diseased only in 6 patients. Primary percutaneous intervention (PCI) was the recommended therapeutic option in 54.1 % of patients but CABG was recommended in 9.6% of patients (Table 3)

Table 3. Diagnosis and coronary angiographic findings of patients undergoing coronary angiography at TASH, Addis Ababa, Ethiopia between May 2017 and June 2023 (n-218)

Variable	Category	Frequency	Percent
Admission diagnosis	CCS	123	56.4
	ACS	95	43.6
CAD	Yes	158	72.5
	No	60	27.5
Premature CAD	Yes	40	18.3
	No	178	81.7
Mature CAD	Yes	118	54.1
	No	100	45.9
Left main lesion	None	212	97.2
	Non-obstructive	1	.5
	Obstructive	5	2.3
LAD lesion	None	85	39.0
	Non-obstructive	17	7.8
	Obstructive	116	53.2

LCX lesion	None	169	77.5
	Non-obstructive	10	4.6
	Obstructive	39	17.9
RCA lesion	None	159	72.9
	Non-obstructive	10	4.6
	Obstructive	49	22.5
PCI	Yes	118	54.1
	No	100	45.9
CABG	Yes	21	9.6
	No	197	90.4

CCS-chronic coronary syndrome, ACS-acute coronary syndrome, CAD-coronary artery disease

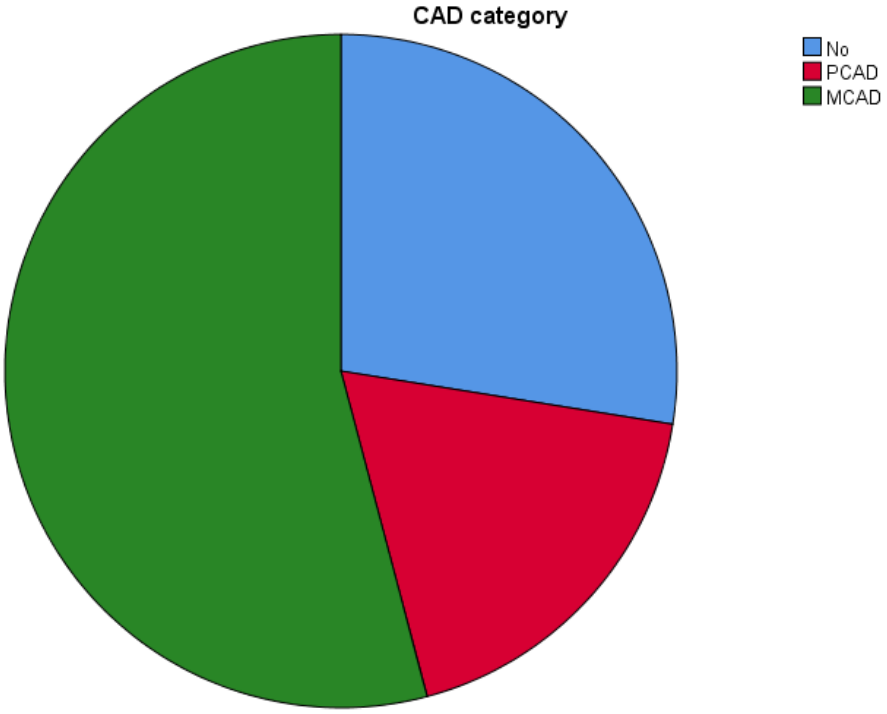

Figure 3- Coronary artery disease category of patients undergoing coronary angiography at TASH, Addis Ababa, Ethiopia between May 2017 and June 2023 (n-218)

Prevalence of premature coronary artery disease

The overall prevalence of premature coronary artery disease among patients who underwent coronary angiography at TASH, Addis Ababa Ethiopia between May 2017 and June 2023 was found to be 18.3%.

Factors associated with premature coronary artery disease

According to multivariate logistic regression male sex, hypertension, low high-density lipoprotein, and admission diagnosis of coronary artery disease were significantly associated with premature coronary artery disease. Male patients were 3.5 times (AOR=3.5,95%CI: 1.492,8.367) more likely to develop premature coronary artery disease as compared to females. Patients with hypertension were 2.8 times (AOR=2.8,95% CI: 1.162,6.767) more likely to have premature coronary artery disease as compared to patients without hypertension.

Additionally, patients with HDL cholesterol <40mg/dl were 2.3 times (AOR=2.306,95% CI:1.025,5.191)more likely to have premature coronary artery disease as compared to patients with HDL level of >=40mg/dl and patients with an admission diagnosis of the chronic coronary syndrome were 2.2 times (AOR=2.220,95%CI: 1.035,4.762) more likely to have premature coronary artery diseases as compared to patients with admission diagnosis of acute coronary syndrome.

The presence of diabetes mellitus. left ventricular hypertrophy on echocardiographic examination and left ventricular systolic dysfunction on echocardiographic examination were not associated with premature coronary artery disease on multivariate logistics regression (table 4).

Age, family history of cardiovascular disease, stroke, CKD, peripheral artery disease, and metabolic panel except HDL were not associated with premature coronary artery disease during bivariate logistic regression screening.

Table 4. Bivariate and Multivariate logistic regression showing factors associated with premature coronary artery disease among patients who underwent coronary angiography at TASH, Addis Ababa, Ethiopia between May 2017 and June 2023(n-218)

Variables	Category	COR	95% C. I	p-value	AOR	95% C. I	p-value
Sex	Male	2.815	1.288,6.150	.009	3.533	1.492,8.367	.004
	Female						
Hypertension	Yes	3.435	1.640,7.197	.001	2.80	1.162,6.767	.022
	No						
Diabetes	Yes	.614	0.303,1.241	.174	1.396	.628,3.102	.413
	No						
HDL	<40	2.133	1.020,4.458	.044	2.306	1.025,5.191	.044
	>=40						
LVH	Yes	0.327	0.137,0.781	.012	1.823	.644,5.163	.258
	No						
LVEF (2)	41-50	0.356	0.136,0.932	.036	.426	.147,1.230	.115
	>50						
Admission diagnosis	CCS	.502	.251,1.006	.052	2.220	1.035,4.762	.041
	ACS						

AOR-adjusted odds ratio, C.I-confidence interval. HDL-high density lipoprotein, LVH -left ventricular hypertrophy, LVEF left ventricular ejection fraction

Discussion

The overall prevalence of premature coronary artery disease among patients who underwent coronary angiography in this study was 18.3% and it was significantly associated with male sex, hypertension, low HDL, and admission diagnosis of chronic coronary syndrome.

This prevalence of premature CAD among patients who underwent coronary angiography is higher than in multicenter, with a large sample size study done in Malaysia at 16% (23) but lower than in the study done in Iraq at 31%(20) as later study excluded patients with normal coronary angiography in the final analysis.

In other studies that used different age cut points and groups of population prevalence of premature coronary artery disease varied significantly depending on the age cut point used and increased as the age cut point increased. The proportion of premature coronary artery disease in < 45-year-old patients in Spain was 9%(22) which is nearly half of our study prevalence and 55% in < 55-year-old males and < 65-year-old women in Malaysia(21)which is threefold to our study.

In this study, premature coronary artery disease was significantly associated with male sex which is similar in studies done in Egypt(12) and Iraq(20) but not in Malaysia although 69.1% of patients were males in the young group(23). Hypertension was another factor that was significantly associated with premature coronary artery disease in this study like studies done in Iraq, India, and Iran (20, 24-27) but not in the USA (11)

Similar to studies done on ACS patients <45 years old in Egypt(12) and Malaysia(21) low HDL was also significantly associated with premature coronary artery disease in this study. Although diabetes(24-27), smoking(11, 12, 20, 23-25, 27), family history of coronary artery disease(11, 12, 20, 21, 27), dyslipidemia(11, 12, 20, 24, 25, 27) and obesity (23)were significantly associated with premature coronary artery disease in other studies it was not true in this study, because only a few patients had a family history of CVD, one-fifth of patients had a history of ever smoking or not currently smoking, and one-tenth of patients were obese as compared to Iraq's 38%(20) and Malaysia's 20.9% (23)study.

The prevalence of smoking in Ethiopia as compared to other countries is low 4.5% in males and 1% in females(29) and family history of cardiovascular disease occurs in only 8.5% of study participants done in eastern Ethiopia(30)

In contrast to other studies, admission diagnosis of chronic coronary syndrome was significantly associated with premature coronary artery disease in this study which may be related to a high proportion of patients with admission diagnosis of chronic coronary syndrome but not acute coronary syndrome.

This study showed that male sex was predominant and two-thirds of patients clustered in the age range of 40-60 years with a mean age of 54.7 years (SD,12.4) and a median age of 55 years which is similar to the previous study done in Ethiopia(19). As compared to other studies done in Ethiopia, hypertension and diabetes were common CVD risk factors identified in this study too but not dyslipidemia (28) although More than half (55.5%) of patients had HDL cholesterol levels < 40mg/dl in this study. Both retrospective and prospective studies done to assess treatment outcome of ACS patients in different tertiary care hospital in Ethiopia showed that most patient were male and hypertension followed by dyslipidemia were most common identified risk factors(15-18).

This is consistent with overall prevalence of cardiovascular risk factors in sub-Saharan Africa where hypertension is more prevalent than, hyperlipidemia ,physical inactivity ,smoking, obesity and diabetes as compared to global and high income countries prevalence(6)

More than half (56.4%) of patients were labeled to have admission diagnosis of chronic coronary syndrome in contrast to a previous study in which acute coronary syndrome was accounting more than half (53.7%) of admissions, although nearly similar 72.5 % and 75.7% of patients had angiographically confirmed coronary artery disease in our study and previous study respectively(19). This difference may emanate from the patient's initial health institution visit and time of coronary angiography intervention such that most patients will come through a referral after passing the acute phase of the acute coronary syndrome and labeled as chronic coronary syndrome in this study.

Limitations; this study was a retrospective cross-sectional, chart review, and single-center study which includes only one-third of patients outside Addis Ababa so difficult to generalize for large population. Additional chronic coronary syndrome was a common admission diagnosis as most

patients underwent elective coronary angiography so difficult to generalized to acute coronary syndrome.

Conclusion and recommendation

The magnitude of premature coronary artery disease at TASH Addis Ababa, Ethiopia is high. Hypertension, male sex, low HDL, and admission diagnosis of chronic coronary syndrome were significantly associated with premature CAD. Tremendous effort should be applied to preventing, detecting, and controlling hypertension and dyslipidemia at community and individual levels.

Annexes

Annex I: Questionnaire to assess prevalence and risk factors of premature coronary artery disease among patients who underwent coronary angiography at TASH, Addis Ababa Ethiopia

1- Sociodemographic profile			
101	Card number		
102	Age in years		
103	Sex	Male _____	Female _____
104	Address	Addis Ababa____	Outside Addis Ababa_____
2-Cardiovascular risk factors			
201	Family history of CAD	Yes _____	No _____
202	History of Hypertension	Yes _____	No_____
203	History of Diabetes	Yes _____	No_____
204	History of Dyslipidemia	Yes_____	No_____
205	Obesity	Yes_____	No_____
206	History of ever Smoking	Yes _____	No_____
207	History of PAD	Yes_____	No_____
208	History of Stroke	Yes_____	No_____
209	History of CKD	Yes _____	No_____
3- Laboratory profile			
301	FBS in mg/dl		
302	HgA1c in %		
303	Total cholesterol in mg/dl		
304	LDL-cholesterol in mg/dl		
305	HDL-cholesterol in mg/dl		

306	Triglyceride in mg/dl		
307	Serum creatinine in mg/dl		
4-ECG and echocardiographic findings			
401	ECG	LVH _____	No LVH_____
402	Echocardiography	LVH_____	N0 LVH____
403	Echocardiography LVEF	Preserved ____	Reduced ____
5- admission diagnosis and coronary angiography findings			
501	Admission diagnosis	Chronic coronary syndrome ___	Acute coronary syndrome ___
502	Coronary artery disease on angiography	Yes ____	No_____
503	Diseased coronary artery	Left main____	LCX____
		LAD____	RCA____
504	The severity of stenosis in %	Left main _____	LCX____
		LAD____	RCA____
505	Complexity of lesion (A, B, C)	Left main _____	LCX____
		LAD____	RCA____
506	Therapeutic options	Medical _____	PCI_____
		CABG____	

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