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Premature Acute Coronary Syndrome and Coronary Artery Disease in Saudi Arabia and the Middle East: Epidemiology, Risk Profiles, Angiographic Patterns, and Clinical Outcomes

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ADMINISTRATIVE INFORMATION**Support** - Self financed.**Review Stage at time of this submission** - Preliminary searches.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202690068

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 September 2026 and was last updated on 15 September 2026.

INTRODUCTION

Review question / Objective What are the prevalent modifiable risk profiles (e.g., dyslipidemia, smoking, khat chewing, metabolic syndrome, type 2 diabetes) and genetic factors (family history) associated with premature acute coronary syndrome (ACS) and coronary artery disease (CAD) in Saudi Arabia and the Middle East?

What are the predominant angiographic patterns and anatomical severity of CAD (e.g., single-vessel vs. multivessel disease, left anterior descending artery involvement, Gensini scores) in young patients compared to older cohorts?

How do short- and long-term clinical outcomes—including in-hospital, 1-month, and 1-year mortality, major adverse cardiovascular events (MACE), revascularization strategies (PCI vs. CABG), and ejection fraction (EF)—differ between young patients with premature ACS/CAD and older or regional reference groups?

Rationale Coronary artery disease (CAD) was traditionally viewed as a disease of old age, but in the Middle East, the age of first myocardial infarction (MI) is 10 to 12 years younger compared to Western countries.

The Middle East and GCC region feature a unique clustering of risk factors. This includes one of the highest global prevalences of type 2 diabetes, a high burden of metabolic syndrome, and high rates of familial hypercholesterolemia and family history due to genetic factors. Furthermore, regional behavioral exposures—such as waterpipe (shisha) smoking and khat chewing (prevalent in Yemen and southwestern Saudi Arabia)—exert strong sympathomimetic effects on the cardiovascular system that standard Western risk models fail to capture.

Existing literature across Saudi Arabia and the region relies heavily on single-center or registry studies with inconsistent diagnostic criteria for premature CAD (e.g., varying age cutoffs ranging from <40\$ to <55\$ years for men and women). This variation has hindered the ability to form a clear, unified regional picture.

Condition being studied Premature Coronary artery disease.

METHODS

Search strategy Searches will be conducted across four electronic databases: PubMed, CINAHL, ScienceDirect, Scopus

A combination of Medical Subject Headings (MeSH) and free-text terms joined by Boolean operators:

Condition: ("acute coronary syndrome" OR "ACS" OR "coronary artery disease" OR "CAD" OR "myocardial infarction")

Age Group: ("premature" OR "young")

Geography: ("Saudi Arabia" OR "Gulf" OR "GCC" OR "Middle East")

Combined Search String: ("premature" OR "young") AND ("acute coronary syndrome" OR "ACS" OR "coronary artery disease" OR "CAD") AND ("Saudi Arabia" OR "Gulf" OR "Middle East").

Participant or population Patients diagnosed with premature ACS or CAD residing in Saudi Arabia, Gulf Cooperation Council (GCC) countries, or other Middle Eastern nations.

Intervention Exposure:

Risk factors specific to or prevalent in the region, including modifiable risk factors (e.g., cigarette smoking, waterpipe/shisha smoking, khat chewing, dyslipidemia, metabolic syndrome, type 2 diabetes) and genetic factors (e.g., family history of premature CAD).

Comparator Older patients with ACS/CAD within the same region or general non-age-stratified regional reference cohorts.

Study designs to be included Observational studies (retrospective cohorts, prospective cohorts, case-control studies, and cross-sectional studies).

Eligibility criteria Studies published between 2022 and 2026

Studies where English is the main language

Studies conducted in Saudi Arabia, GCC countries, or the Middle East

Human subjects with premature ACS or CAD (typical cutoffs: ≤ 40 to ≤ 50 years for men; < 45 to < 55 years for women).

Information sources Mainly published studies in given databases.

Main outcome(s) Primary: In-hospital, 1-month, and 1-year mortality; major adverse cardiovascular events (MACE).

Secondary: Angiographic severity (single-vessel vs. multivessel disease, LAD involvement), revascularization strategies (PCI vs. CABG), and left ventricular ejection fraction (LVEF).

Quality assessment / Risk of bias analysis

Informal quality assessment for observational studies will be conducted based on the domain categories of the Newcastle-Ottawa Scale (NOS):

Selection of study cohorts or cases/controls.

Comparability of exposed and unexposed groups or age cohorts.

Assessment of outcomes or ascertainment of exposure.

Risk Classification Strategy:

Multi-center registries will generally be categorized as having low-to-moderate risk of selection bias due to broader sampling.

Single-center retrospective studies using convenience sampling from catheterization laboratories will be categorized as having moderate-to-high risk of selection bias.

Strategy of data synthesis Due to substantial methodological heterogeneity (varying age cutoffs, diverse observational study designs, and varying operational definitions across settings), a quantitative meta-analysis will not be performed. Instead, a narrative synthesis structured around three main domains will be presented:

Risk Profiles: Regional-specific and traditional cardiovascular risk factor comparisons.

Angiographic Patterns & Revascularization Strategies: Anatomical burden of disease and clinical procedures performed.

Clinical Outcomes: Comparison of mortality, LVEF, and adverse event profiles between young cohorts and older comparator groups.

Subgroup analysis Comparisons among distinct age bands within the young cohort, such as comparing patients aged under 40 years, 40 to 45 years, and over 45 to 50 years.

Evaluation of premature presentation and outcome differences between male and female cohorts, including specific female-only thresholds (e.g., women ≤ 50 or < 55 years vs. men ≤ 45 or < 40 years).

Sensitivity analysis Testing whether risk factor distributions (e.g., dyslipidemia, khat use) and outcomes remain consistent when altering the operational definition of "premature" CAD

Assessing the stability of narrative findings by comparing conclusions derived strictly from Saudi

Arabian single-country cohorts against multi-country regional registries across the GCC and broader Middle East.

Language restriction English.

Country(ies) involved Saudi Arabia.

Keywords coronary artery disease, CAD, acute coronary syndrome, ACS, myocardial infarction, premature, Saudi Arabia, Middle East, GCC.

Contributions of each author

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