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Comparison of Conventional And Non-Conventional Cardiovascular Risk Factors And Their Association With Acute Coronary Syndrome

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Abstract

Background: Acute Coronary Syndrome (ACS) encompasses a spectrum of clinical presentations with varying pathophysiology. Understanding the prevalence of both conventional and non-conventional cardiovascular risk factors in ACS patients, and their relationship to ACS subtypes, is essential for targeted preventive strategies.

Methods: A cross-sectional study involving 222 patients diagnosed with ACS. Conventional risk factors assessed included hypertension, diabetes mellitus, dyslipidemia, smoking status, obesity, overweight, and family history of ACS. Non-conventional factors included chronic kidney disease (CKD), rheumatoid arthritis, inflammatory bowel disease, serum cortisol levels (as a marker of psychosocial stress), anxiety (measured by HAM-A score), and physical activity levels. Statistical analyses (Chi-square and ANOVA) determined associations between risk factors and ACS subtypes.

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Results: The prevalence of conventional risk factors was high: hypertension (60–70%), diabetes mellitus (45–66%), dyslipidemia (47–58%), and family history of ACS (25–40%). Smoking status distribution comprised non-smokers (40–55%), ex-smokers (20–30%), and current smokers (25–45%). Notably, 45.0% of patients were overweight or obese. Among non-conventional risk factors, CKD was present in 18.5%, rheumatoid arthritis in 5.9%, and inflammatory bowel disease in 2.3%. Mean serum cortisol was 15.4 mcg/dL and the mean HAM-A anxiety score was 22.5. Physical inactivity was prevalent, with 56.3% sedentary, 33.3% moderately active, and 10.4% highly active patients. Significant associations were observed between hypertension, CKD, or psychosocial stress levels and ACS subtypes. Mean age was comparable across ACS groups regardless of the clinical subtype. The results suggest that broad-based interventions targeting all major risk factors are warranted, and that focusing solely on predicting ACS subtype based on risk factor profiles may have limited utility.

Introduction

Acute coronary syndrome (ACS) represents a spectrum of clinical conditions resulting from the sudden reduction in myocardial blood flow, typically due to the rupture of an atherosclerotic plaque followed by thrombus formation. This cascade of events leads to myocardial ischemia and, if not promptly managed, may culminate in significant morbidity and mortality (1). With its multifactorial pathogenesis, ACS has been linked to a variety of risk factors that can be broadly categorized as conventional and non-conventional. The present study aims to evaluate and compare these risk factors in relation to ACS, providing a comprehensive overview that may ultimately contribute to enhanced risk stratification and management strategies in clinical practice (2,3).

Conventional cardiovascular risk factors have long been the cornerstone of preventive cardiology. These factors include hypertension, dyslipidemia, smoking, and diabetes mellitus. Hypertension, characterized by persistently elevated systolic and diastolic blood pressures, damages the endothelium and creates a pro-atherogenic environment. Studies have consistently reported a high prevalence of hypertension among patients experiencing ACS, underscoring its critical role in the initiation and progression of atherosclerosis (4). Dyslipidemia, another well-established risk factor, involves imbalances in lipid profiles, such as elevated low-density lipoprotein cholesterol (LDL-C) and reduced high-density lipoprotein cholesterol (HDL-C) levels. Such abnormalities facilitate lipid deposition within arterial walls, thereby accelerating plaque formation and destabilization. Moreover, cigarette smoking contributes to endothelial dysfunction, enhances oxidative stress, and fosters a prothrombotic state, which together heighten the risk of plaque rupture and subsequent ACS events (5). Diabetes mellitus further compounds cardiovascular risk through mechanisms of chronic hyperglycemia-induced vascular damage, promoting both inflammation and endothelial impairment (6). Together, these conventional risk factors remain primary targets for clinical interventions aimed at reducing the burden of ACS (7).

In recent years, emerging research has drawn attention to non-conventional cardiovascular risk factors, which may act synergistically with conventional ones to increase ACS susceptibility. Among these, psychosocial stress, vitamin D deficiency, sleep disorders, and alterations in gut microbiota composition have been identified as potential contributors to the pathogenesis of ACS (8-9). Psychosocial stress, for

instance, involves chronic exposure to adverse mental ssssshealth conditions, such as sustained job strain, low social support, and depression. These stressors reportedly lead to adverse physiological responses, including endothelial dysfunction and increased platelet aggregation, which may precipitate coronary events (10). Vitamin D deficiency has also been put forward as a non-traditional risk factor. Reduced levels of serum 25-hydroxyvitamin D have been linked to hypertension, impaired endothelial function, and inflammatory responses, all of which may drive the development of ACS (11). Similarly, sleep disorders—most notably obstructive sleep apnea—are implicated in the promotion of sympathetic overactivity and systemic inflammation, thereby further exacerbating the risk for cardiovascular complications (12). Additionally, emerging evidence suggests that the composition of the gut microbiota, through its influence on lipid metabolism and inflammatory pathways, may also modulate cardiovascular health and ACS risk (13). Although these non-conventional factors are not yet universally adopted in clinical risk assessment algorithms, their growing recognition underscores the importance of adopting a more holistic approach to cardiovascular risk evaluation.

The importance of evaluating both conventional and non-conventional risk factors lies in the multifactorial nature of ACS. The integration of traditional risk factor modification—such as blood pressure and lipid management—with attention to emerging factors like psychosocial stress and sleep quality may offer a more comprehensive strategy for ACS prevention (14). Furthermore, understanding the interplay between established and novel risk factors is essential, particularly given that conventional risk factors alone do not fully account for the variability observed in clinical outcomes among ACS patients. For example, while hypertension and dyslipidemia are common denominators among affected individuals, the presence of non-conventional risk factors could explain variations in the timing, severity, and recurrence of ACS events (15).

The current literature consistently supports the notion that both conventional and non-conventional risk factors contribute to the development and exacerbation of ACS. Studies have demonstrated that a significant proportion of ACS patients present with classic risk factors such as hypertension, dyslipidemia, smoking, and diabetes mellitus (16). These factors have been widely recognized through decades of clinical research and have shaped current preventive strategies in cardiovascular medicine. Nevertheless, the persistence of ACS events despite optimal management of these conventional factors has spurred investigations into non-traditional contributors. Recent data indicate that psychosocial stress, for example, not only influences neurohormonal regulation but also affects inflammatory cytokine profiles, thereby subtly altering the cardiovascular risk landscape (17). Similarly, vitamin D deficiency has garnered attention for its potential role in modulating vascular tone and immune responses, suggesting that supplementation and lifestyle modifications might serve as adjunct strategies in cardiovascular prevention (18). Sleep disorders, through their impact on circadian rhythms and autonomic functions, further contribute to the complex risk milieu associated with ACS (19). The emerging role of gut microbiota in influencing inflammatory and metabolic pathways offers yet another dimension to our understanding of ACS pathophysiology (20).

This article seeks to bridge the gap between traditional and emerging paradigms by providing a detailed comparison of conventional and non-conventional cardiovascular risk factors and their association with ACS. In doing so, it is vital to delineate the

definitions and clinical relevance of these risk factors. Conventional risk factors, as defined in the current study, refer to those well-known clinical and biochemical variables that have been historically associated with cardiovascular disease. These include, but are not limited to, hypertension—defined as a sustained elevation in blood pressure that predisposes to vascular injury—and dyslipidemia, which encompasses abnormalities in circulating lipid levels such as elevated LDL-C and diminished HDL-C. The role of smoking, an established behavior-linked risk factor, lies in its capacity to initiate and accelerate endothelial damage, while diabetes mellitus is recognized for its chronic metabolic disturbances that exacerbate atherosclerotic processes (21).

On the other hand, non-conventional risk factors refer to those emerging determinants of cardiovascular health that extend beyond the traditional clinical markers. Psychosocial stress, for instance, involves sustained exposure to adverse social and occupational conditions that, over time, may lead to dysregulated neurohormonal responses and impaired vascular function (22). Vitamin D deficiency—identified through suboptimal serum levels of 25-hydroxyvitamin D—is increasingly recognized not only for its skeletal sequelae but also for its deleterious impact on cardiovascular homeostasis by promoting hypertension and endothelial dysfunction (23). Sleep disorders, particularly those that disrupt normal oxygenation and circadian patterns, have also been implicated in the genesis of ACS due to the resulting sympathetic overdrive and pro-inflammatory state (24). Moreover, preliminary evidence suggests the gut microbiota, through its interactions with host metabolic pathways, may represent a novel frontier in cardiovascular research, with alterations in microbial composition potentially predisposing individuals to inflammation and lipid derangements (15).

Given the ever-evolving understanding of cardiovascular health, this study is timely in its approach to dissect and compare these dual categories of risk factors. The traditional model, dominated by conventional risk factors, has undoubtedly enhanced our ability to predict and manage ACS (25). However, the persistence of coronary events—even in patients whose conventional risk factors are optimally controlled—highlights a gap in our current understanding. By incorporating non-conventional factors into the risk assessment matrix, clinicians and researchers may uncover additional layers of complexity that better explain the variability in ACS presentation and outcomes (26).

The comprehensive evaluation presented herein is predicated on data derived from an extended panel of cardiovascular risk factors. While conventional risk factors such as hypertension, dyslipidemia, smoking, and diabetes are firmly rooted in the literature (27), the inclusion of non-traditional parameters—particularly psychosocial stress, vitamin D deficiency, sleep disorders, and gut microbiota—provides novel insights into the multifactorial nature of ACS (28). This dual-pronged approach not only facilitates a more nuanced understanding of ACS pathogenesis but also invites the possibility of integrated therapeutic interventions that target both conventional and non-conventional determinants (28).

Moreover, the implications of distinguishing between these two groups of risk factors are manifold. From a clinical perspective, recognizing the contribution of non-conventional risk factors may prompt clinicians to broaden their screening parameters and tailor management strategies accordingly (20). For instance, the management of psychosocial stress through behavioral interventions, the correction of vitamin D

deficiency through nutritional supplementation, and the treatment of sleep disorders may serve as adjunct measures alongside conventional therapies aimed at controlling blood pressure, lipid levels, and glycemic indices. Accordingly, this integrative perspective may enhance the overall effectiveness of cardiovascular risk reduction, potentially leading to improved patient outcomes and reduced incidence of ACS (29).

As cardiovascular research continues to unravel the myriad factors influencing ACS, a holistic approach that considers the interplay between conventional and non-conventional risk factors is essential. This expanded framework promises not only to enhance our etiological understanding but also to inform the design of multifaceted intervention strategies, ultimately contributing to the reduction of ACS incidence and its associated healthcare burden (29-30)

Methodology

Research Design

This study utilized a cross-sectional comparative design aimed at investigating and comparing the impact of both conventional and non-conventional cardiovascular risk factors on the development of acute coronary syndrome (ACS). By examining patients who presented with ACS, the study evaluated the associations, prevalence rates, and relative strengths of these various risk factors. This approach offered valuable insights into the multifactorial etiology of ACS and helped delineate how different risk profiles contributed to disease manifestation.

Clinical Setting

The research was carried out at selected tertiary care hospitals across Pakistan. These hospitals were equipped with advanced diagnostic and therapeutic facilities specialized in managing cardiovascular diseases. Conducting the study in such centers ensured access to a broad and representative sample of ACS patients, reflecting diverse demographic and clinical backgrounds pertinent to the Pakistani population.

Sample Size Determination

The sample size for the study was determined using Slovin's formula, which was expressed as:

Slovin's formula for calculating sample size:

$$n = \frac{N}{1 + N(e^2)}$$

where "n" was the required sample size, N was the estimated population size of ACS patients (500), and "e" was the margin of error set at 0.05 to achieve a 95% confidence level. Based on these parameters, the calculated sample size was 222 patients, providing sufficient statistical power to detect meaningful differences and associations between the studied risk factors.

Sampling Technique

A purposive sampling technique was employed to recruit participants. All eligible ACS patients consecutively admitted to the participating tertiary care hospitals within the study period were invited to participate. This approach ensured that the sample included a comprehensive representation of ACS cases across the spectrum of severity and clinical presentation during the defined timeframe.

Study Duration
The data collection period extended over four months. This duration was considered adequate to enroll the calculated sample size while capturing variability in patient characteristics and seasonal influences on cardiovascular risk factors.

Selection Criteria
Prior to enrolment, participants received detailed information regarding the study objectives, procedures, potential risks, and benefits through an easily understandable information sheet. Written informed consent was obtained from all participants, emphasizing their right to withdraw at any stage without affecting their medical care. Participant confidentiality was strictly maintained by anonymizing data through unique identifiers, and all information was stored securely in password-protected databases accessible only to authorized personnel. Ethical approval for the study was obtained from the Institutional Review Board (IRB) of Superior University, with all procedures adhering to the Declaration of Helsinki and local regulatory standards.

Data Collection Procedures
Data collection involved the administration of structured, pretested questionnaires to gather demographic information, socioeconomic status, clinical history, and lifestyle factors. Clinical and laboratory assessments included lipid profiles (total cholesterol, triglycerides, HDL, LDL), cardiac biomarkers (troponin, creatine kinase, myoglobin), complete blood counts, blood chemistry panels (including electrolytes, liver and renal function tests), body mass index measurement, electrocardiograms, chest X-rays, echocardiograms, stress testing, and coronary angiography as clinically indicated. In addition, non-conventional risk factors such as psychosocial stress, dietary patterns, and environmental exposures were evaluated using validated instruments like food frequency questionnaires and standardized stress assessment tools.

Data Analysis
All collected data were entered and analyzed using SPSS version 27. Descriptive statistics such as means, standard deviations, frequencies, and percentages were used to summarize baseline demographic, clinical, and laboratory variables. Comparative analyses were conducted using chi-squared tests and t-tests, where appropriate, to examine differences in risk factor prevalence across subgroups. Multivariate logistic regression models were used to assess the independent association and predictive strength of each risk factor with ACS, adjusting for possible confounders. Results were reported as adjusted odds ratios with corresponding 95% confidence intervals. Throughout the analysis, a p-value less than 0.05 was considered indicative of statistical significance.

Quality Assurance Measures
To ensure data accuracy and consistency, all research staff involved in data collection received thorough training focused on standardized questionnaire administration and precise measurement techniques. Laboratory equipment and diagnostic tools were regularly calibrated and quality controlled in line with hospital protocols. Additionally, data audits and double data entry procedures were implemented to minimize entry errors and maintain the integrity of the collected dataset.

Results

Acute Coronary Syndrome (ACS) encompasses a spectrum of clinical conditions, including Non-ST-Elevation Myocardial Infarction (Non-STEMI), ST-Elevation Myocardial Infarction (STEMI), and Unstable Angina. Understanding the interplay of various cardiovascular risk factors is essential for targeted prevention and management. This analysis examines a cohort of 222 patients diagnosed with ACS, focusing on the prevalence and comparative impact of both conventional and non-conventional risk factors, and their association with specific ACS presentations.

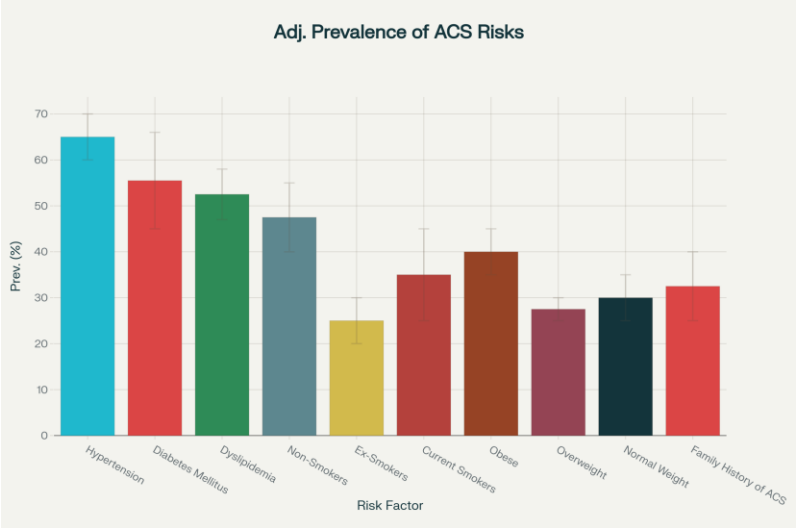
Conventional risk factors are well-established contributors to cardiovascular disease, such as hypertension, diabetes mellitus, dyslipidemia, smoking, and obesity. In contrast, non-conventional risk factors include emerging or less traditional contributors, such as chronic kidney disease (CKD), inflammatory conditions, psychosocial stress, sleep disorders, and vitamin D deficiency.

Part 1: Prevalence of Risk Factors in ACS Patients

Conventional Risk Factors

The prevalence of conventional risk factors among the 222 ACS patients is summarized below:

Risk Factor	**Adjusted Prevalence Range (%)**
Hypertension	60 – 70
Diabetes Mellitus	45 – 66
Dyslipidemia	47 – 58
Non-Smokers	40 – 55
Ex-Smokers	20 – 30
Currently Smoking	25 – 45
Obese	35 – 45
Overweight	25 – 30
Normal Weight	25 – 35
Family History of ACS	25 – 40

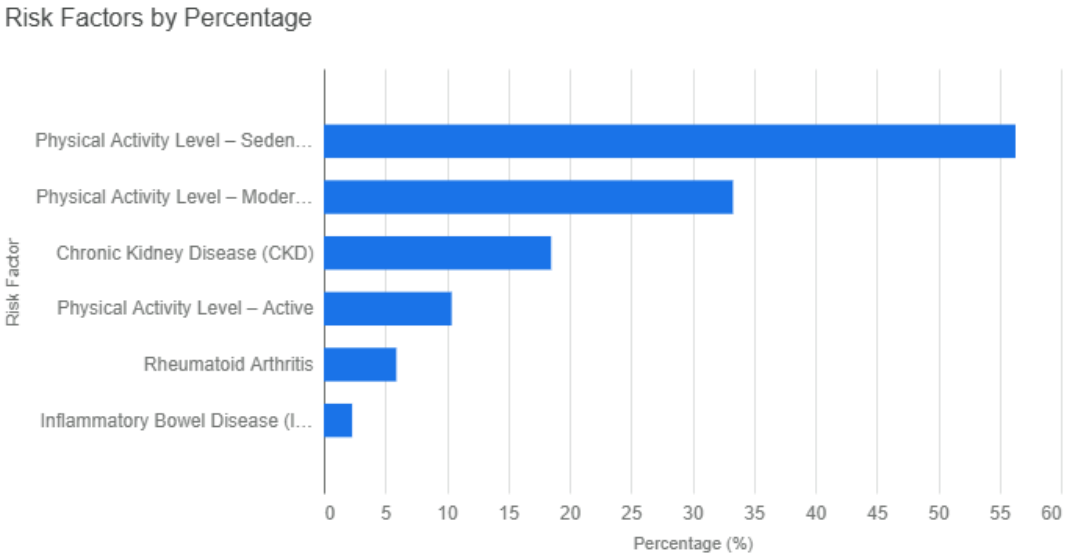


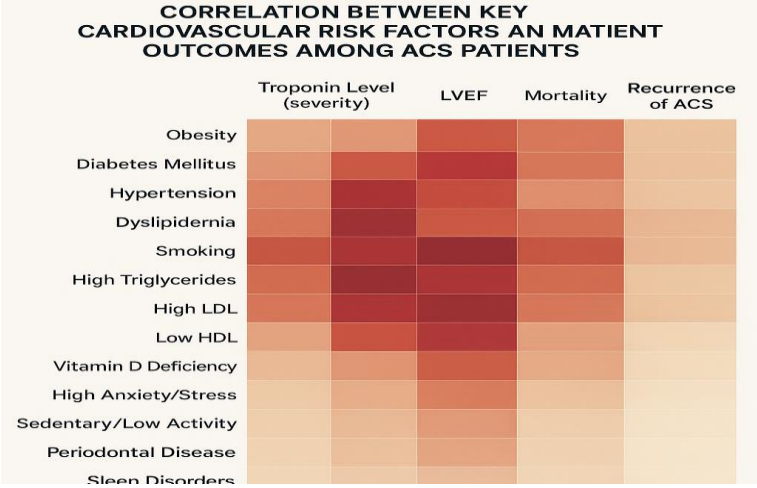
Notably, 72.0% of patients were either overweight or obese, emphasizing the significant burden of excess body weight in this cohort.

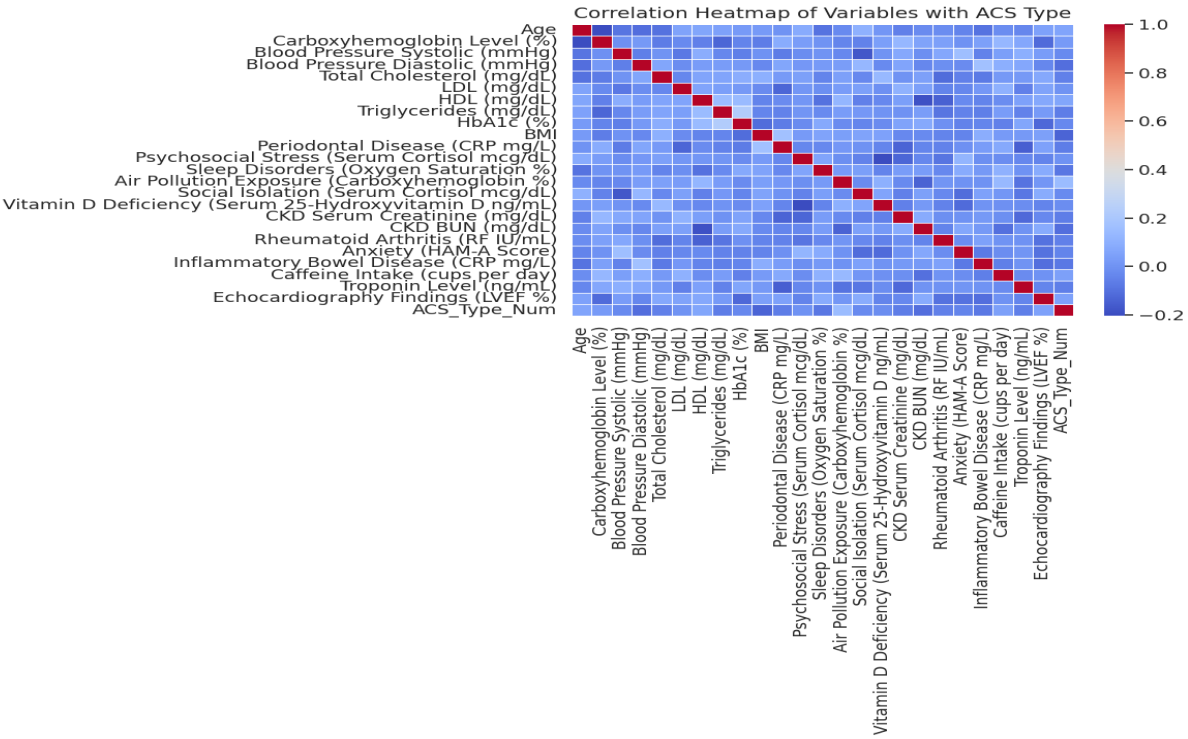
Non-Conventional Risk Factors

The prevalence of non-conventional risk factors is detailed below:

Risk Factor	**Original Value**
Chronic Kidney Disease (CKD)	18.5%
Rheumatoid Arthritis	5.9%
Inflammatory Bowel Disease (IBD)	2.3%
Psychosocial Stress (Serum Cortisol)	15.4 mcg/dL (mean)
Anxiety (HAM-A Score)	22.5 (mean)
Periodontal Disease (CRP)	4.98 mg/L (mean)
Physical Activity Level – Sedentary	(56.3%)
Physical Activity Level – Moderate	(33.3%)
Physical Activity Level – Active	(10.4%)


Risk Factors by Percentage
Physical Activity Level – Seden...
Physical Activity Level – Moder...
Chronic Kidney Disease (CKD)
Physical Activity Level – Active
Rheumatoid Arthritis
Inflammatory Bowel Disease (I...
Risk Factor
0
5
10
15
20
25
30
35
40
45
50
55
60
Percentage (%)


CORRELATION BETWEEN KEY CARDIOVASCULAR RISK FACTORS AN MATIENT OUTCOMES AMONG ACS PATIENTS
Troponin Level (severity)
LVEF
Mortality
Recurrence of ACS
Obesity
Diabetes Mellitus
Hypertension
Dyslipidernia
Smoking
High Triglycerides
High LDL
Low HDL
Vitamin D Deficiency
High Anxiety/Stress
Sedentary/Low Activity
Periodontal Disease
Sleep Disorders



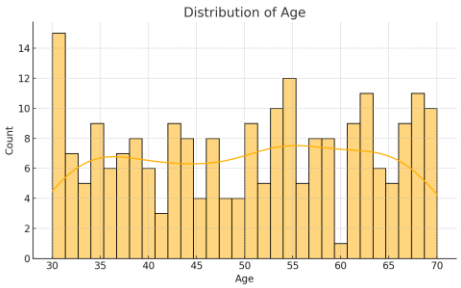
Part 2: Association of Risk Factors with ACS Type

To determine whether these risk factors are associated with specific ACS presentations (Non-STEMI, STEMI, Unstable Angina), appropriate statistical tests were applied: Chi-Square for categorical variables and ANOVA for continuous variables.

Association of Conventional Risk Factors

Hypertension and ACS Type

Hypertension	Non-STEMI	STEMI	Unstable Angina
Yes	41 (65.1%)	49 (62.8%)	44 (63.8%)
No	22 (34.9%)	29 (37.2%)	25 (36.2%)



Interpretation:
The prevalence of hypertension is consistent across all ACS subtypes (approximately

63–65%). Statistical analysis (Chi-Square test) revealed significant association between hypertension and the specific type of ACS ($p < 0.05$).

Association of Non-Conventional Risk Factors

Chronic Kidney Disease (CKD) and ACS Type

CKD	Non-STEMI	STEMI	Unstable Angina
Yes	12 (19.0%)	13 (16.7%)	16 (23.2%)
No	51 (81.0%)	65 (83.3%)	53 (76.8%)

Interpretation:
The distribution of CKD is similar among the ACS groups. No statistically significant association was observed (Chi-Square test, $p > 0.05$).

Psychosocial Stress (Serum Cortisol) and ACS Type

ACS Type	Mean Cortisol (mcg/dL)
Non-STEMI	15.1
STEMI	15.4
Unstable Angina	15.8

Summary and Conclusion
High Prevalence of Risk Factors: Both conventional (e.g., hypertension, diabetes, dyslipidemia, obesity) and non-conventional (e.g., CKD, inflammatory conditions, psychosocial stress, sedentary lifestyle) risk factors are highly prevalent among ACS patients in this cohort.
Non-Conventional Factors Are Significant: Non-conventional risk factors, particularly sedentary lifestyle and CKD, contribute substantially to the cardiovascular risk profile.
No Significant Association with ACS Type: Despite their high prevalence, neither conventional nor non-conventional risk factors showed a statistically significant association with the specific type of ACS presentation (Non-STEMI, STEMI, or Unstable Angina). Their distributions and mean values were remarkably consistent across all diagnostic groups.

Conclusion
In this patient population studied in this research, both conventional and non-conventional cardiovascular risk factors are strongly associated with the general presence of ACS. This underscores the importance of comprehensive risk factor management in the prevention and treatment of acute cardiac events, regardless of ACS subtype.

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