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Gender-based Differences in Young Indian Patients with Acute Coronary Syndrome: A Comprehensive Analysis

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ABSTRACT

Objectives: The steep rise in acute coronary syndrome (ACS) cases among young adults, particularly those ≤ 45 years old, poses a significant concern, especially in India. This study delved into the baseline characteristics, risk factors, and echocardiographic and angiographic profiles of ACS patients under 45 years of age, with a focus on discerning gender-based differences.

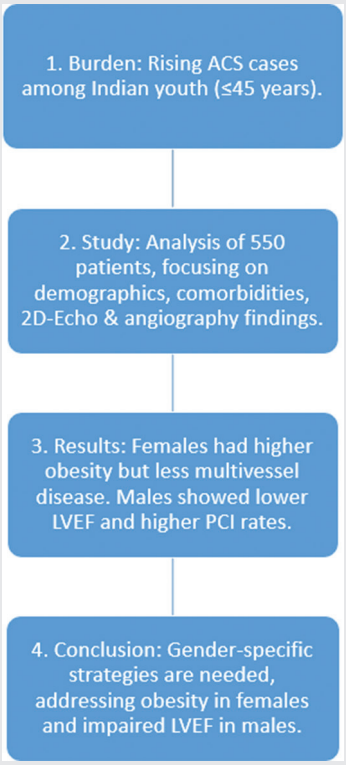
Materials and Methods: A retrospective, observational cohort study was conducted, including young adults aged 18–≤45 years diagnosed with ACS who underwent coronary angiography. Demographic, clinical, and angiographic data were meticulously analyzed.

Results: Our study of 550 young ACS patients (mean age: 40.2 ± 4.7 years) from January 2018 to July 2023 found that females, forming nearly 10% of the cohort, had a higher obesity prevalence (38.7% vs. 56.9%, $P = 0.012$). Multivessel disease was less common in females ($P < 0.0001$). Left anterior descending (67.3%) and right coronary (41.3%) arteries predominantly affected, seen in significantly higher proportion of males ($P = 0.003$ and $P = 0.011$, respectively). Left ventricular ejection fraction ≤40% was notably lower in males ($P = 0.029$). Percutaneous coronary intervention (PCI) was the primary treatment modality (59.3%), with significantly lower rates among females (43.1% vs. 60.9%, $P = 0.040$).

Conclusion: Despite the increasing prevalence, research on gender differences in young adults with ACS is limited, especially in the Indian population. We observed higher obesity rates in females compared to males, along with lower rates of multivessel disease in females. Males had lower ejection fractions and underwent PCI more often than females. These findings highlight the need for gender-specific approaches and tailored interventions in ACS management.

Keywords: Acute coronary syndrome, Young, Gender, India

ABSTRACT IMAGE



INTRODUCTION

Acute coronary syndrome (ACS), a pressing global health issue, has seen a notable uptick in prevalence, especially among young adults in South Asian countries like India. In fact, a significant portion of coronary artery disease cases in India occurs in individuals under 45 years of age, with nearly a quarter of anterior myocardial infarction cases happening in those under 40.[1] Despite this surge, there is a glaring lack of gender-based disparity studies within this demographic. Global studies and registries report a 7–10.3% prevalence of ST-elevation myocardial infarction in young adults, depending on age cut-offs, and highlight gender-based differences in outcomes.[2] While research elsewhere has shed light on gender differences in ACS, such investigations are notably absent in India, where unique sociocultural, genetic, and environmental factors may influence cardiovascular health differently. A recent study in the US population revealed gender disparities in ACS patients, underlining the urgency of investigating such phenomena in specific populations.[3] Addressing this gap, our study aims to thoroughly analyze clinico-demographic factors and coronary angiography (CAG) profiles among young ACS patients (<45 years) in India, with a keen focus on potential gender differences. By uncovering nuanced differences in ACS presentation and outcomes among males and females, this research endeavors to inform tailored interventions aimed at mitigating the burden of cardiovascular disease in the Indian population.

MATERIALS AND METHODS

This single-center retrospective study was conducted at a tertiary care cardiology center in Central India. The data collection was started after approval from the local institutional ethics committee, i.e., Criticare hospital and research institute – EC/CHRI/24/65 on July 22, 2024. The study was conducted following ethical principles of the Declaration of Helsinki, good clinical practice guidelines, and applicable local regulations.

CAG and 2D-echocardiography (2D-ECHO) were performed by trained cardiologists following hospital protocols. Angiographic measurements were made by visual estimation by two cardiologists. A diameter stenosis of 50% in coronary segment was considered significant.

We reviewed medical records of 550 young adults (18–≤45 years) diagnosed with ACS between January 2018 and July 2023. Information on demographics, comorbidities, addiction history, laboratory parameters, 2D-ECHO, and CAG findings was recorded in Microsoft Excel.

Table 1: Baseline characteristics.

Baseline characteristics	Total (*n*=550)	Male (*n*=499)	Female (*n*=51)	*P*
Age (years)	40.2±4.7	40.1±4.8	41.3±3.2	0.080
18–30	25 (4.5)	25 (5.0)	0	0.202
31–40	199 (36.2)	182 (36.5)	17 (33.3)	
41–45	326 (59.3)	292 (58.5)	34 (66.7)	
Co-morbidities				
Obesity	222 (40.4)	193 (38.7)	29 (56.9)	0.012
Hypertension	213 (38.7)	190 (38.1)	23 (45.1)	0.327
Diabetes mellitus	167 (30.4)	150 (30.1)	17 (33.3)	0.628
Stressful work	14 (2.5)	13 (2.6)	1 (2.0)	0.781
Addictions				
Tobacco Only	12 (2.2)	12 (2.4)	0	0.250
Smoking and Tobacco both	59 (10.7)	56 (11.2)	3 (5.9)	
Alcohol	59 (10.7)	55 (11.0)	4 (7.8)	0.485
Laboratory parameters				
Total cholesterol (*n*=221) (mg/dL)	164.0 (138–194.5)	165 (138–195)	156 (126.5–199.0)	0.717
LDL-C (*n*=212) (mg/dL)	98 (72.5–122.2)	98.6 (71.8–122.4)	89.6 (74.4–121.8)	0.764
Serum Triglyceride (*n*=195) (mg/dL)	134 (95–197)	134 (96–197)	101 (58–157)	0.252
Serum Creatinine (*n*=477) (mg/dL)	1.0 (0.86–1.15)	1.02 (0.89–1.16)	0.78 (0.68–0.89)	<0.001
Left ventricular ejection fraction	48.7±11.1	48.4±11.1	52.0±10.3	0.029
≤40%	159 (28.9)	151 (30.3)	8 (15.7)	0.076
41–50%	161 (29.3)	145 (29.1)	16 (31.4)	
>50%	230 (41.8)	203 (40.7)	27 (52.9)	
Regional wall motion abnormality				
Absent	221 (40.2)	192 (38.5)	29 (56.9)	0.026
Anterior	169 (30.7)	159 (31.9)	10 (19.6)	
Inferior	117 (21.3)	110 (22.0)	7 (13.7)	
Anterior+inferior	23 (4.2)	22 (4.4)	1 (2.0)	
Other	20 (3.6)	16 (3.2)	4 (7.8)	

LDL-C: Low-density lipoprotein cholesterol

Table 2: Coronary angiographic findings and treatments.

Parameters	Total (*n*=550) (%)	Male (*n*=499)	Female (*n*=51)	*P*
No. of vessels involved				
Single vessel disease	271 (49.1)	248 (49.7)	23 (45.1)	<0.0001
Double vessel disease	142 (25.7)	133 (26.7)	9 (17.6)	
Triple vessel disease	95 (17.2)	91 (18.2)	9 (7.8)	
Normal coronaries	42 (7.6)	27 (5.4)	15 (29.4)	
Major vessels involved				
Left anterior descending artery	370 (67.3)	346 (69.3)	24 (47.1)	0.011
Right coronary artery	227 (41.3)	216 (43.3)	11 (21.6)	0.003
Left circumflex artery	169 (30.7)	157 (31.5)	12 (23.5)	0.242
Obtuse marginal artery	99 (18.0)	95 (19.0)	4 (7.8)	0.047
Diagonal artery	86 (15.6)	78 (15.6)	8 (15.7)	0.992
Left main artery	79 (14.4)	71 (14.2)	8 (15.7)	0.777
Ramus artery	75 (13.6)	71 (14.2)	4 (7.8)	0.206
Treatments				
Medical management	213 (38.7)	186 (37.3)	27 (52.9)	0.040
PCI	326 (59.3)	304 (60.9)	22 (43.1)	
CABG	11 (2.0)	9 (1.8)	2 (3.9)	

PCI: Percutaneous coronary intervention, CABG: Coronary artery bypass grafting

Clinical follow-up data were collected through clinic visits or telephonic interviews. No routine angiographic follow-up was conducted. ACS was defined by typical clinical symptoms, relevant electrocardiographic changes, and/

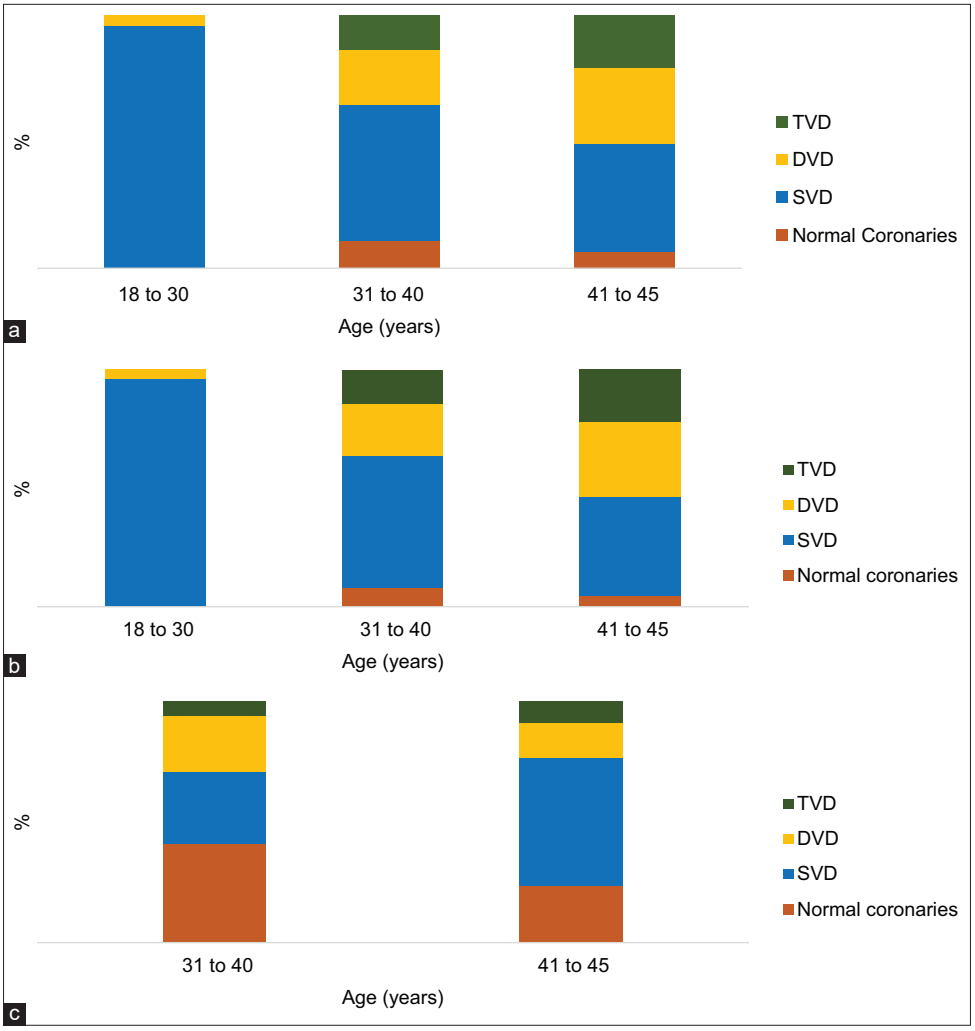


Figure 1: Distribution of vessel involvement by patient age. (a) Total sample, (b) Males, (c) Females. (a) The Y-axis represents the percentage (%) of the total sample size (males + females combined). (b) The Y-axis represents the percentage (%) of the total number of males in the study. (c) The Y-axis represents the percentage (%) of the total number of females in the study.

or elevated troponin T or troponin I. All deaths were considered cardiac in origin unless a clear non-cardiac cause could be established. All patients had at least a 1-year follow-up unless they died within that year. For deceased patients, next of kin were interviewed and death certificates reviewed.

Analysis was performed using Microsoft Excel. We reported frequencies, proportions, and measures of central tendency for categorical and continuous variables, respectively. We used the Chi-square test for categorical data and either a student *t*-test or Mann–Whitney U-test for continuous data based on the data distribution. Significance for all comparisons was set at 5% (i.e., $P < 0.05$).

RESULTS

Baseline characteristics

The study population's baseline characteristics are summarized in Table 1. The mean age was 40.2 ± 4.7 years, with 59.3% aged above 40 years. Around 10% of females developed ACS. Obesity, hypertension, and diabetes were prevalent in 40.4%, 38.7%, and 30.4% of patients, respectively. Gender-wise analysis showed no age distribution difference ($P = 0.202$). Obesity was significantly higher in females (38.7% vs. 56.9%, $P = 0.012$). Serum triglycerides showed non-significantly higher median values in males ($P = 0.252$), while serum creatinine was significantly higher ($P < 0.001$)

Table 3: Characteristics of patients with mortality outcome.

Parameters	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age	45	45	34	41	45	45
Gender	F	M	M	M	M	M
Diabetes	Yes	No	No	Yes	Yes	No
LVEF	50	45	55	60	60	40
CAG Profile	DVD	DVD	SVD	TVD	SVD	SVD
PCI	No	Yes	No	No	Yes	No

LVEF: Left ventricular ejection fraction, CAG: Coronary angiography, PCI: Percutaneous coronary intervention, SVD: Single vessel disease, TVD: Triple vessel disease, DVD: Double vessel disease

in males. On 2D-ECHO, males had significantly lower mean left ventricular ejection fraction (LVEF) than females (48.4 ± 11.1% vs. 52.0 ± 10.3%, $P = 0.029$). While LVEF categories did not significantly differ between genders ($P = 0.076$), more males had LVEF ≤40% (30.3% vs. 15.7%). Males also showed significantly higher regional wall motion abnormality (RWMA) rates ($P = 0.026$).

Coronary angiographic findings and treatment

Table 2 illustrates coronary angiographic findings and treatments. Single vessel disease (SVD) was most common, followed by double vessel disease (DVD) and triple vessel disease (TVD). Males had higher rates of DVD (26.7% vs. 17.6%) and TVD (18.2% vs. 7.8%) ($P < 0.0001$). Left anterior descending artery involvement was significantly higher in males (69.3% vs. 47.1%, $P = 0.011$). Medical management was more common in females, while males predominantly underwent PCI ($P = 0.040$).

Distribution of vessel involvement by age

Figure 1a provides the distribution of vessel involvement identified on CAG by the patient's age. In age group 18–30 years, SVD and DVD were present in 96% and 4% of patients, respectively. In 31–40-year age group, SVD (53.8%) was most common followed by DVD (22.2%), and TVD (13.6%) while 10.6% had normal coronaries. In age 41–45 years, SVD, DVD, and TVD were seen in 42.9%, 29.8%, and 20.9% of patients, respectively. Figure 1b demonstrated vessel involvement by age in males. As seen from the distribution of proportions, it was statistically significant ($P < 0.0001$) with DVD and TVD occurring at a greater frequency in above 30-year age groups. Among males, SVD (96%) was most common in 18–30-year age. In males above 40 years, 31.5% had DVD and 22.3% had TVD. Figure 1c shows the same in females. None of the female below 30 years of age had ACS. In 31–40-year age females, SVD, DVD, and TVD were seen in 29.4%, 23.5%, and 5.9%, respectively. Similarly, in 41–45 years of females, these were seen in 52.9%, 14.7%, and 8.8%, respectively, with no statistically significant differences ($P = 0.359$).

Major cardiovascular outcomes

With a telephonic follow-up, 497 patients responded. Each of the patient was inquired for the major cardiovascular events (MACE), hospitalizations, revascularization, and mortality. Within 1 year of ACS diagnosis, mortality occurred in six (1.2%) patients. Among the six cases [Table 3], five were males, above the age of 40 years, and three were diabetic. On CAG, SVD, DVD, and TVD were noted in 3, 2, and 1 patient, respectively. Two cases had undergone PCI.

DISCUSSION

ACS poses a significant global health challenge with varied impacts across demographics. Our discussion compares our study's findings with existing literature, focusing on gender differences in young Indian ACS patients. We explored patients up to 45 years old, with a mean age of 40.2 years. Traditional risk factors such as obesity, hypertension, and diabetes mellitus were prevalent, aligning with earlier Indian studies.[4] However, our study showed higher diabetes mellitus prevalence compared to some Western populations.[5] Notably, obesity was significantly more prevalent among females, emphasizing the need for gender-specific risk assessment and management strategies.[6] Metabolic factors, such as obesity, diabetes, and hypertension, play a significant role in cardiovascular disease, as highlighted by the coronary artery disease in the young registry from India.[7] Higher obesity rates in Indian females may stem from cultural norms that restrict physical activity for women, especially in urban areas, combined with diets high in carbohydrates and low in balanced nutrients. In addition, the higher prevalence of polycystic ovary syndrome (PCOS) among young Indian females, a condition linked to obesity and insulin resistance, contributes to this trend. In our study, approximately 10% of young women were diagnosed with ACS, consistent with rates in Indian studies 9.86–12.9%,[8,9] but lower than in the West 15.8–26%,[10,11] likely due to differing lifestyle factors. Single-vessel disease prevailed in nearly 50% of young adults with ACS, similar across genders as in other Indian studies,[12,13] also aligning with findings in older adults. We also observed exclusively SVD in individuals aged 18–30, with a progressive

increase in multivessel disease prevalence beyond the age of 30 in both genders. Notably, a higher proportion of females exhibited normal coronary arteries, indicating potential non-atheromatous ACS. Males had a lower mean LVEF than females, with 30.3% having LVEF ≤40% compared to 15.7% of females. Indian males tend to have lower LVEF due to higher rates of smoking, hypertension, and diabetes, along with genetic factors such as insulin resistance and central obesity, which accelerate atherosclerosis. These factors contribute to early vascular aging, leading to reduced LVEF at younger ages compared to males in Western populations. Western men with ACS often show better LVEF due to proactive hypertension management and lifestyle differences. In addition, 40.2% of patients showed no RWMA on ECHO, with females notably more absent of RWMA than males, highlighting potential gender-related differences.

In ACS treatment, options include medical management or procedures like percutaneous coronary intervention (PCI) or coronary artery bypass grafting. Our study found around 60% opting for PCI, influenced by factors like financial constraints, especially in India. Studies from Kuwait and Spain reported PCI rates from 32% to 52%.[14,15] indicating regional treatment differences. While our findings align with some Western studies on gender disparities in ACS, differences exist, with Western populations having higher lifestyle-related risk factors.[16] Indian patients may have a distinct risk profile, influenced by metabolic syndrome and cultural factors affecting healthcare-seeking behavior.[17,18]

Although young adults with ACS comparatively have lower rates of MACE than older adults,[11,19] the risk persists for the worse outcomes. Readmission and recurrent cardiovascular events are reported in young ACS as well. Smoking, diabetes, hypertension, no use of stents, and lower LVEF are identified as important predictors of such events.[14,20] Mortality rate is lower as seen in our study. Studies from Kenya (1.5%) and Saudi Arabia (0.9%)[21] reported similar mortality rates. Over nearly 9-year follow-up, a study in Israeli young ACS patients observed mortality rate of 9.1%.[20,22] Thus, identification of possible factors that contribute to MACE outcomes is essential in young ACS patients.

The observed gender differences in young ACS patients may stem from complex interactions among hormonal, genetic, and lifestyle factors. Higher ACS prevalence in young Indian males is influenced by genetic predispositions for early-onset atherosclerosis and a greater frequency of lifestyle risk factors such as smoking and alcohol use and pro-inflammatory state which accelerate cardiovascular aging. In contrast, the protective effects of estrogen in females delay atherosclerosis onset, offering relative protection against early cardiovascular events compared to males. Highlighting these gender-specific findings could lead to tailored ACS management strategies in India, with a focus on targeted prevention for young males, i.e., smoking cessation programs and early screening for hypertension and on the other hand, metabolic health interventions such as PCOS and obesity for females, ultimately enhancing outcomes in resource-limited settings.

Our study has limitations, primarily due to its retrospective nature, which inherently entails design constraints. Other limitations include a smaller sample size compared to Western studies, the potential influence of confounding variables, and possible bias in follow-up. Long-term prospective follow-up to document major cardiovascular outcomes like heart failure or recurrent ACS, finding gender specific risk factors including emotional behaviors which could offer valuable clinical insights into young ACS.

CONCLUSION

In summary, our study highlights significant gender differences in young Indian ACS patients, mirroring but also differing from Western populations. In our study of ACS in young Indians, most patients were over 40 years old. Notably, females showed higher rates of obesity and received PCI less often, with no female patients presenting with ACS below 30 years of age. Males, on the other hand, showed a significantly higher prevalence of multivessel disease and lower LVEF. These findings highlight important gender-based disparities in the presentation and management of young ACS patients, underscoring the need for tailored strategies in clinical practice.

Ethical approval

The data collection was started after approval from the local institutional ethics committee, i.e., Criticare hospital and research institute – EC/CHRI/24/65 on July 22, 2024.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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