International Journal of Research in Medical Sciences
Selvaganesh M et al. Int J Res Med Sci. 2024 Jul;12(7):2340-2345
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20241880

Original Research Article

Acute coronary syndrome in very young adults (<35 years of age) - time to awake and act! A prospective analytical study from South India

Selvaganesh M.[1]*, Saravanan R. R.[1], Satheeshkumar S.[1], Siva Kumar G. S.[1], Veeramani S. R.[2], Arul A. S.[3], Balasubramanian S.[1]

[1]Department of Cardiology, Velammal Medical College Hospital and Research Institute, Madurai, Tamil Nadu, India
[2]Department of Cardiology, Dindigul Medical College, Dindigul, Tamil Nadu, India
[3]Department of Cardiology, Tirunelveli Medical College, Tirunelveli, Tamil Nadu, India

Received: 12 March 2024
Revised: 04 April 2024
Accepted: 15 June 2024

***Correspondence:**
Dr. Selvaganesh M.,
E-mail: selvapacemaker@gmail.com

ABSTRACT

Background: Acute coronary syndrome in very young adults (<35 yrs) was considered as an uncommon entity, recently shows rising incidence especially in India. Hence we planned this study with the aim, to investigate the incidence, clinical, angiographic profile and outcome of ACS in this population.
Methods: This is a prospective analytical study included patient <35 yrs with ACS admitted to cardiology department in a tertiary hospital of South India. Risk factors, clinical, angiographic profile and follow up data were recorded and analyzed.
Results: Among the total 2180 patients with ACS, 5.8% (n=127) were very young adults. Youngest one was 11 yrs old with coronary anomaly. Median age was 30yrs (SD±3) and only 8.6% (n=10) were obese. Smoking, male sex were the major conventional risk factors followed by low HDL (52%). Family history of premature coronary event seen in 12.9%, hyperhomocysteinemia, elevated LPA and high fibrinogen were observed in 15%, 20% and 3.5% respectively. Anterior wall MI with LAD occlusion was the commonest type (66.3%). Angiographically 31.4% (36/116) had recanalised vessels, coronary anomaly was seen in 3 (2.5%) patients and pure ectasia in 4 (3.4%) patients. Only 2 were undergone primary PCI (1.7%), 61% (n=71) received thrombolytic therapy. Median delay for angiogram was 72 hrs (3 days). In-hospital mortality was 3.4% and 4.5% (n=5) during follow up.
Conclusions: The incidence of ACS among very young adults is on the rising trend (5.8%). Obstructive CAD in 56.9% patients implies the rapid progression of atherosclerosis. With little contribution of novel risk markers of atherosclerosis, smoking and dyslipidemia accelerate the process of premature vascular aging in Indian subcontinent.

Keywords: Acute coronary syndrome, Precocious ACS, South India, Very young adults, ≤35 yrs

INTRODUCTION

Cardio vascular diseases are emerging as a major health hazard in South Asia. Especially India is in the fourth stage of epidemiological transition where in Non Communicable Diseases (NCD) showing rising trend in incidence whereas communicable diseases are declining. As per WHO statistics in 2014, CVD contributed to 26% of total mortality in India.[1] According to the previous studies South Asians particularly Indians are vulnerable for CAD and presents with Acute Coronary syndrome at younger age (<40 yrs). Acute myocardial infarction at an age <40 yrs is defined as young MI and accounts for 25% of all AMI in Indians.[2,3] Very few studies analyzed ACS in very young adults (<35yrs). Morbidity and mortality due to ACS at this productive age group impose huge

emotional and economical impact on the family. Data regarding the conventional, novel risk factors in this age group with ACS is limited.[4] Outcome analysis also scarce. Objectives of the study were to study the angiographic characteristics and outcome in very young ACS population <35 years and to compare with patients above 35 years. Also, to study the prevalence conventional risk factors in very young ACS population <35 years presenting with ACS and compare with the remaining patients with ACS. Additionally, to study prevalence of novel risk factors in these young patients with ACS (≤35 yrs).

METHODS

This is a prospective analytical study conducted in a tertiary cardiac care centre Madurai Medical college and Government Rajaji Hospital in South India during the period 2012-2014.

Inclusion criteria

All the patients who admitted with the diagnosis of acute coronary syndrome [ST Elevation Myocardial Infarction (STEMI), Non STEMI, unstable angina] were included in the study.

Exclusion criteria

Those who had previous history of ACS, or percutaneous coronary interventions, coronary artery bypass graft surgery and those with cardiomyopathies, valvular heart diseases, congenital heart disease, chronic renal, liver diseases were excluded. Patients with preexisting cardiac arrhythmias also excluded from the study.

Out of the 2180, patients who fulfilled the inclusion and exclusion criteria 127 patients were 35 or younger than 35 years of age classified as cases, remaining 2053 (>35 years) were categorized as controls. The institutional ethical clearance was obtained. A detailed history taking along with physical examination were done for both cases and control group. At the time of admission, electrocardiogram ECG and Troponin I were done for the evaluation of ACS. Based on ECG and Troponin assay both groups were classified as different ACS types (STEMI, NSTEMI, UA). With ECG echocardiogram, area of myocardial involvement recognized (ASMI - Anteroseptal AWMI-Anterior Wall, IWMI -Inferior Wall Myocardial infarction). Complete blood count and biochemical investigations were done to exclude renal and liver dysfunction. Conventional risk factors such as gender, family history of premature CAD, smoking, diabetes mellitus, hypertension, dyslipidemia, were evaluated as per definition and compared between the groups. The body mass index (BMI) assessed as per QUETLET index.

Diabetes mellitus: Anybody taking treatment for DM or having HbA1C >6.5, FBS fasting blood sugar ≥126 mg%, post prandial blood sugar ≥200% were defined as having diabetes mellitus as per American diabetes Association Guidelines.[5] Patients with BMI ≥25 is defined as overweight, ≥30 is labelled as obese. Dyslipidemia is defined as low HDL cholesterol <50 mg% in males, 40 mg% for females, LDL cholesterol >130mg% triglycerides >150 mg% non HDL cholesterol >130 mg%. Systemic hypertension was defined as any body having BP >140/90 mm of Hg or on antihypertensive therapy. Family history of premature CAD deemed to present if any of these patients first degree relatives had ACS <55 yrs of age in males or, 65 yrs in females. Three novel risk factors, homocysteine, lipoprotein a(Lpa), fibrinogen were assessed in very young adults not in others. Lp(a) level more than 30 mg% homocysteine level >15 µmol/L were considered abnormal. Considering the acute phase effect of fibrinogen, sample for fibrinogen was taken during follow up visit at 3rd month. Plasma level >300 mg /dl is considered as hyperfibrinogenemia. Coronary angiography (CAG) was done in both groups through the right radial or femoral route after taking patient's consent. Significant CAD was defined as 70% or more narrowing of a major coronary artery. According to the epicardial coronary arteries (left anterior descending artery [LAD], left circumflex artery, and right coronary artery [RCA]) involvement grouped into single (SVD), double-(DVD), and triple-vessel disease (TVD).

Statistical analysis

Statistical analyses were performed using the SPSS for windows Continuous variables were expressed as mean ± standard deviation whereas categorical variables were as percentages. Comparison between the groups was done by Chi-square test for categorical variables at the level of significance $\alpha = 0.05$ ($P<0.05$).

RESULTS

Among the 2180 patients with ACS 127 persons were very young adults constitutes 5.8% of overall ACS. Mean age is 29.7±4.7 years. Youngest one was only 11 yrs old with coronary anomaly. Male preponderance was noted in both groups, out of 127 very young adults 93.8% (n=119) were males, only 6.2% (n=8) were females. Mean delay to reach the hospital was 7 hrs SD ±3 hrs. Only 61% received thrombolytic therapy either in our institution or nearby hospital. Streptokinase was the commonest lytic agent used, primary PCI was performed only in 2%. Coronary angiogram performed in 118 very young adults with mean delay of 3 days.

ST Elevation MI (STEMI) was the commonest type of ACS in both groups, of them majority had anterior wall MI. Baseline variables tabulated in Table 1.

Angiographic profile was tabulated in Table 2 obstructive CAD (stenosis >70%) was noted in 56.9% of very young adults (n=67) and 77.6% of other group (>35 yrs). Single

vessel disease involvement is the most common angiographic pattern in both groups (66.3% vs 42% in >35 yrs p<0.00001). Triple vessel involvement with more number of type B, type C lesion were observed in adult >35yrs (23.7% vs 6.4% p <0.001) (Table 3). About 1/3, n=37 (31.4%)of very young adults had recanalised vessels as evidenced by non-obstructive CAD (<50% stenosis) with or without thrombus.

Table 1: Baseline variables.

Variables	Age ≤35 yrs % (n=127)	Age > 35 yrs % (n=2053)
Risk factors		
Age in years (SD)	29.7 (±4.7)	56 (±7.2)
Sex (Males)	92.9 (118)	72
Smoking	73.2	67
Diabetes mellitus	5	59
Systemic hypertension	8	42
Obesity	8.6	56
Family H/o premature CAD	12.5	16
Lipid profile		
Total cholesterol (>200 mg %)	11 (14) 180±32 mg%	20.5 (423) 186±31 mg%
Triglycerides (>150 mg%)	36.2 (46) 138±36 mg%	42.8 (880) 146±24mg%
LDL >130mg%)	27.6 (35) 116±28 mg%	41 (842) 122±25 mg%
HDL (<50 mg% in females <40 mg % in males)	52 (66) 40±16 mg%	39.7 (8050 41±17 mg%
STEMI	66.6	60.2
NSTEMI	27.3	28
UA	6.1	11.8

Table 2: Angiographic profile of very young adults (≤35 yrs).

Angiographic profile	Cases (n=118)	Percent
Obstructive CAD	67	56.9
Recanalised vessel non obstructive CAD	37	31.4
Normal coronaries	5	4.2
Coronary anomaly	3	2.5
Ectasia	4	3.
Dissection	2	1.7

After male sex, smoking was the major risk factor followed by dyslipidemia. Among the lipid abnormalities low HDL was the predominant one observed in 52% (n=66) of very young adults compared with others 39.7%%. Other lipid abnormalities were elevated total cholesterol (11% vs 20.5%), elevated TGL (36.2 vs 42.8%), and increased LDL (27.6 vs 41%).

Table 3: Comparison of angiographic severity.

Angiographic severity	Very young ≤ 35 yrs (%)	Adult >35 yrs (%)	P value
SVD	66.3	42	<0.00001
DVD	27.4	34.3	NS
TVD	6.4	23.7	<0.001

Diabetes mellitus, systemic hypertension, and obesity were less commonly observed in younger population as depicted in Table 4. Family h/o premature CAD was observed in 12.6% of younger patients vs 16% in >35 yrs adults. Novel risk factors were estimated only in younger population, elevated levels of homocysteine, Lp(a), fibrinogen level were seen in 15%, 20% 13.5% respectively Table 5.

Table 4: Comparative analysis of risk factors.

Variables	Age ≤35 yrs % (n=127)	Age >35 yrs % (n=2053)	P value
Risk factors			
Sex (Males)	92.9 (118)	72 (1478)	<0.00001
Smoking	73.2 (93)	67.6 (1388)	0.187883
Diabetes mellitus	5.5 (7)	58.9 (1211)	<0.00001
Systemic hypertension	9.4 (12)	42.2 (866)	<0.00001
Obesity	8.6 (11)	56 (1150)	<0.00001
Family H/o premature CAD	12.6 (16)	16.1 (332)	0.286033
Lipid profile			
Total cholesterol (>200 mg%)	11 (14)	20.5 (423)	0.008868
Triglycerides (>150 mg%)	36.2 (46)	42.8 (880)	0.1416
LDL >130mg%)	27.6 (35)	41 (842)	0.002695
HDL (<50 mg% in females <40 mg % in males)	52 (66)	39.7 (805)	0.006246

Table 5: Prevalence of novel risk factors in very young adults.

Novel risk factors	N (%)
Hyperhomocysteinemia	15
Lipoprotein (a)	20
Hyper fibrinogen	13.5

Regarding the outcome analysis, clinical events HF (12.6% vs 16%), in hospital mortality, 6 month mortality (3.2 vs 4%, 4.7 vs 6% respectively) were not much different between the groups. Embolic events are more

common among very young adults (6.3% vs 3%) (Figure 1).

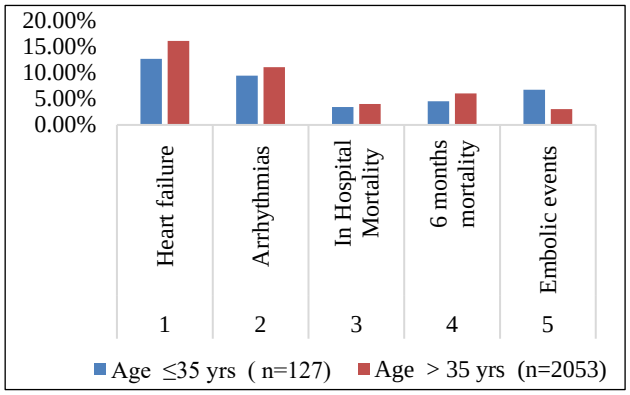

Figure 1: Comparison of clinical outcome between groups.

DISCUSSION

The prevalence of CAD in India was showing exponential increase from 1% during 1960[6] to 12.5% during 2016.[7] South Indians were documented to have 60% higher prevalence of CAD than North Indian (13% vs 8%) as studied by Singh et al.[8] Indians are vulnerable to develop AMI at an younger age, about 5-10 years earlier than the western population. The age limit for defining the spectrum of young CAD varies from 35 to 55 years. CAD occurring in less than 40 years is defined as premature CAD, acute coronary syndrome in very young adults <35 yrs is considered as precocious ACS.[9]

Once ACS in patients less than 35 yrs was considered rare. But recent evidence indicated that ACS in less than 35 yrs contributes to 3-5.8% (current study). Coronary atherosclerosis the denominator of CVD, begins in early life. Bogalusa heart study demonstrated that considerable number of young adults between 21-39 yrs of age have evidence of fatty streaks (85%), raised fibrous plaques (69%), which has been proved by an IVUS based study.[10,11] Multitude of factors were speculated for this rapid progression for atherosclerosis.

Angiographic evaluation of our patients revealed significant obstructive CAD in 56.9% of very young patients ≤35 years. Non-obstructive CAD with or without thrombus and normal coronaries observed in 31.4%, 4.2% respectively. Earlier studies by Glover et al, Kaul et al reported obstructive CAD in 78%, 76.9% respectively.[12] But the cut off used for obstructive CAD was >50% angiographic stenosis of any one major coronary artery. Studies during 21st century revealed obstructive CAD in 59.8%, 80%.[4] Our population concurs with other studies in the clinical, angiographic profile showing STEMI the most common presentation and SVD is the commonest angiographic finding (66.3 vs 42%) with LAD involvement in majority. Triple vessel disease more commonly seen in control groups (6.4 vs 23.7%).

Considering dual face of angiographic findings (obstructive and non obstructive), both atherogenic and thrombogenic mechanism may play role in the pathogenesis of ACS in these very young patients. As evidenced from our study along with available literature we postulate that atherosclerosis and its complication seems to be the major pathophysiological mechanism for ACS in these very young adults.

Even in those with non obstructive CAD, atherosclerotic plaque of insignificant in size but probably having vulnerable plaque morphology with or without underlying thrombomodulatory dysfunction may responsible for the ACS. This insignificant plaque could have been well demonstrated with intravascular ultra sound.

Like other studies males predominantly involved (92.9% vs 72%), with male to female ratio (13:1). Male to female ratio varies from (9-20:1).[13,14] The protective role of estrogen in the reproductive age group females is well known in preventing the progression of atherosclerosis. Among the conventional risk factors male sex, smoking and dyslipidemia especially low HDL are strongly associated with our very young patients compared to adults >35yrs (92.9% vs 72%, 73.2% vs 67.6%, 52% vs 39.7%) respectively. Other risk factors DM, SHT obesity were less commonly observed in study group, 5.5 vs 58.9%, 9.4 vs 42.2%, 8.6% vs 56% respectively (P value <0.00001). Previous studies also highlighted that next to male sex, smoking (78%, 71%) dyslipidemia is the commonest conventional risk factors in AMI patients <35 yrs.[4,15] Among the lipid abnormalities significant younger adults have low HDL compare to other group 52 vs 39.7%, P =0.006). Elevated triglycerides, total cholesterol, LDL was noted in significant numbers even though comparatively less than control group [36.2 vs 42.8% (P value 0.14 NS), 11 vs 20%, 27.6 vs 41%, P value <0.008, <0.002 respectively]. But obesity was less frequent (8.6%) among very young adults. Except studies from west and some studies from Asia most studies reported obesity is less frequent (<20%) among the target group.[9,16] Significant lipid abnormality seen with very young adults especially low HDL elevated triglycerides.

Individuals without obesity but with lipid and metabolic abnormalities constitutes the phenotype termed Normal Weight Dyslipidemia (NWD) which is more common among South Asian.[17] South Asian phenotype (thin but metabolically obese) is generally have elevated TGL and low HDL, normal LDL but have more atherogenic small LDL (atherogenic dysipidemia). Smoking along with atherogenic dyslipidemia might explain the rapid progression of atherosclerosis and significant obstructive CAD in younger patients, (atherogenic mechanism of Young ACS) when compare to control group (patients >35 yrs).

Homocysteine, lipoprotein a (Lpa), and fibrinogen were observed in 15%, 20% 13.6% respectively. Hyperhomocysteinemia is considered as a major risk factor for ACS in young adults reported in 19.2-58.5%.[4,17] In our study homocysteinemia is less prevalent, probable reason is majority of study group ate non-vegetarian diet. After a long existing controversy, recently the casual role of LPa in CVD has been approved by research scientists, with the convincing evidence from genetic, epidemiologic, pathophysiological studies. Positive results also seen from clinical studies moving the focus to therapeutic trials of LPa.[18] Serum fibrinogen is one of the acute phase reactants. Zairis et al and Pineda et al found significantly elevated levels of fibrinogen in ACS population.[19,20] But still independent role of fibrinogen as a cardiovascular risk factor remains controversial as stated in PRIME and ARIC study. Recently in a Chinese study among AMI patients <35 yrs, association between fibrinogen level and severity of stenosis was demonstrated. We speculate that these three novel risk factors accelerate the vascular aging (premature atherosclerosis) by prothrombotic and inflammatory mechanism. They also precipitate ACS by inducing endothelial injury, enhances thrombus formation by platelet activation and interfering with coagulation, fibrinolytic mechanism.

In hospital, 6 month mortality of young patients are not much different from adults >35 yrs (3.2 vs 4%, 4.7 vs 6% respectively). Embolic events are common in younger patients than in control group. Despite less complex angiographic profile clinical outcome similar in both the groups. These productive age group need to be on at least three drugs antiplatelet hypolipidemic drugs ± β blockers and ACE inhibitors.

This study has few limitations. Dietary, physical activity, psychosocial factors were not assessed. Second, risk factors not compared with normal controls. Third, novel Risk factors not assessed with adults >35 yrs. Forth, intravascular imaging would have shed light on the pathogenesis of ACS in these very young adults.

CONCLUSION

Angiographic profile of our study indicates premature vascular aging due to rapid progression atherosclerosis in our very young adults (<35 yrs). Progression of atherosclerotic process is accelerated by smoking in vulnerable young adults with lipid abnormality. Interaction between the abnormal lipids and inflammation defines the progression of atherosclerosis. This interaction is amplified by oxidized phospholipid containing apoB100 lipoprotein (LPa) and proinflammatory and prothrombotic action of Hcy and fibrinogen. More than 30% of young adults had minimal atherosclerosis or normal coronaries. In these population thrombus formation might have been enhanced by two mechanism. 1) Platelet, endothelial dysfunction due to smoking and homocysteine 2) competitive inhibition of plasminogen activity by Lpa.

ACS in very young adults (≤ 35yrs) is not so rare as in the past contributing to 5.8% of overall numbers. Angiographically significant number patients have obstructive coronary artery disease (56.9%) indicate the rapid progression of atherosclerosis in these budding adults. Smoking along with dyslipidemia are the most common modifiable risk factors. Screening, educative and preventive measures to be implemented from adolescent age to protect these productive population.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. World Health Organization. Global Status Report on Noncommunicable Diseases, 2014. Available at: https://iris.who.int/bitstream/handle/10665/148114/9789241564854_eng.pdf?sequence=1. Accessed 01 March 2024.
2. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): Case-control study. Lancet. 2004;364(9438):937-52.
3. Sharma M, Ganguly NK. Premature coronary artery disease in Indians and its associated risk factors. Vasc Health Risk Manag. 2005;1(3):217-25.
4. Sinha SK, Krishna V, Thakur R, Kumar A, Mishra V, Jha MJ, et al. Acute myocardial infarction in very young adults: a clinical presentation, risk factors, hospital outcome index, and their angiographic characteristics in North India-AMIYA Study. ARYA Atheroscler. 2017;13:79-87.
5. Care D. Standards of medical care in diabetes 2019. Diab Care. 2019;42(Suppl 1):S124-38.
6. Mathur KS. Environmental factors in coronary heart disease: an epidemiologic study at Agra (India). Circulation. 1960;21(5):684-9.
7. Krishnan MN, Zachariah G, Venugopal K, Mohanan PP, Harikrishnan S, Sanjay G, et al. Prevalence of coronary artery disease and its risk factors in Kerala, South India: a community-based cross-sectional study. BMC Cardiovasc Disord. 2016;16(12):1-2.
8. Begom R, Singh RB. Prevalence of coronary artery disease and its risk factors in the urban population of South and North India. Acta Cardiolog. 1995;50(3):227-40.
9. Davidson L, Wilcox J, Kim D, Benton S, Fredi J, Vaughan D. Clinical features of precocious acute coronary syndrome. Ame J Medi. 2014;127(2):140-4.
10. Berenson GS, Srinivasan SR, Bao W, Newman WP, Tracy RE, Wattigney WA. Association between

multiple cardiovascular risk factors and atherosclerosis in children and young adults. N Engl J Medi. 1998;338(23):1650-6.
11. Tuzcu EM, Kapadia SR, Tutar E, Ziada KM, Hobbs RE, McCarthy PM, et al. High prevalence of coronary atherosclerosis in asymptomatic teenagers and young adults: evidence from intravascular ultrasound. Circulation. 2001;103(22):2705-10.
12. Glover MU, Kuber MT, Warren SE, Vieweg WV. Myocardial infarction before age 36: risk factor and arteriographic analysis. Ame J Cardiol. 1982;49(7):1600-3.
13. Sricharan KN, Rajesh S, Rashmi, Meghana HC, Badiger S, Mathew S. Study of acute myocardial infarction in young adults: Risk factors, presentation and angiographic findings. J Cli Diagnos Res. 2012;6(2):257-60.
14. Garoufalis S, Kouvaras G, Vitsias G, Perdikouris K, Markatou P, Hatzisavas J, et al. Comparison of angiographic findings, risk factors, and long term follow-up between young and old patients with a history of myocardial infarction. Int J Cardiol. 1998;67(1):75-80.
15. Christus T, Shukkur AM, Rashdan I, Koshy T, Alanbaei M, Zubaid M, et al. Coronary artery disease in patients aged 35 or less-a different beast?. Heart Views. 2011;12(1):7-11.
16. Kalimuddin M, Ahmed N, Badiuzzzaman M, Ahmed MN, Dutta A, Banik D, et al. AMI in very young (aged≤ 35 years) Bangladeshi patients: Risk factors & coronary angiographic profile. Clin Tri Regul Sci Cardiol. 2016;13:1-5.
17. Højland Ipsen D, Tveden-Nyborg P, Lykkesfeldt J. Normal weight dyslipidemia: is it all about the liver?. Obesity. 2016;24(3):556-67.
18. Rallidis LS, Pavlakis G, Foscolou A, Kotakos C, Katsimardos A, Drosatos A, et al. High levels of lipoprotein (a) and premature acute coronary syndrome. Atheroscl. 2018;269:29-34.
19. Zairis MN, Adamopoulou EN, Manousakis SJ, Lyras AG, Bibis GP, Ampartzidou OS, et al. The impact of hs C-reactive protein and other inflammatory biomarkers on long-term cardiovascular mortality in patients with acute coronary syndromes. Atheroscl. 2007;194(2):397-402.
20. Pineda J, Marín F, Marco P, Roldán V, Valencia J, Ruiz-Nodar JM, et al. Premature coronary artery disease in young (age< 45) subjects: interactions of lipid profile, thrombophilic and haemostatic markers. Int J Cardiol. 2009;136(2):222-5.

Cite this article as: Selvaganesh M, Saravanan RR, Satheeshkumar S, Siva Kumar GS, Veeramani SR, Arul AS, et al. Acute coronary syndrome in very young adults (<35 years of age) - time to awake and act!!!-a prospective analytical study from South India. Int J Res Med Sci 2024;12:2340-5.