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ACUTE CORONARY SYNDROME (ACS) RISK FACTORS AND ITS MANIFESTATIONS IN YOUNG PATIENTS: A MULTICENTER STUDY

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ABSTRACT

Objectives: To determine the conventional and non-conventional ACS risk factors in young patients, their associations, and to determine the various manifestations of ACS in young patients.

Study Design: Multi Center Cross Sectional Study.

Place and Duration of Study. Tertiary care hospitals of KPK from May to Oct 2024.

Materials and Methods: This multicenter study was conducted over six months. A total of 139 young acute coronary syndrome (ACS) patients of both genders were included using convenience sampling, while acute myocardial infarction or unstable angina resulting from graft blockage, coronary aneurysms, congenital heart diseases, and severe co-morbid conditions were excluded. After ethical approval, data was collected using a pre-designed questionnaire and analyzed using SPSS and Excel.

Results: The majority (64%) were male and the mean age was 39.69±4.40. Chest pain (87.8%) and anterior MI (27%) were common. STEMI was identified in the majority (46%) and more in males. Hypertension, family history, and dyslipidemia were common. Conventional risk factors were more prevalent in males, STEMI, and in the 36-40 years age range, while chest radiation exposure was found higher (57.9%) in females, and diabetes among NSTEMI and 41-45 age group patients. Urea and ESR had a significant impact on STEMI, while RBS and ESR on NSTEMI. Mild PAH and mild LV systolic dysfunction were common and mean EF (%) was lower in NSTEMI ACS.

Conclusion: STEMI was a common ACS manifestation and hypertension was most prevalent. Smoking and radiation exposure were significantly associated with gender, while urea, and ESR significantly impact ACS manifestations. Mean EF was significantly different among ACS types. Nevertheless, early recognition of risk factors and proper management can prevent ACS progression.

Keywords: Acute coronary syndrome, STEMI, NSTEMI, Risk factors, Young

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INTRODUCTION

Cardiovascular diseases (CVDs) are the leading public health burden causing high morbidity, mortality, health costs and still increasing worldwide, total CVDs almost doubled (271 million to 523 million) and mortality has increased from 12.1 million to 18.6 million from 1990 to 2019 (1) and in 2019 globally greater than 6 million deaths between 30-70 years age and 1.2 million death among young and middle- aged adults (<50 years of age) were due to CVDs (2).CVDs are the leading cause of deathin Asia, in 2019, account for 35% of all deaths in the region, with 10.8 million fatalities and Notably, 39% of these deaths occurred in individuals under 70 years of age, higher than the global average of 34%, United States (23%) and Europe (22%), the majority of CVD-related deaths in Asia (47%) were due to IHD, and the proportion of CVD deaths in Asia increased from 23% to 35%, rising from 5.6 million in 1990 to 10.8 million in 2019 (3,4). In South Asia CVDs are the most common cause of death (35.5%) and Pakistan has the second highest CVDs morbidity (9.74 per 1000 person-years) after Bangladesh but the mortality rate is highest (15.45 per 1000 person-years) than Asian countries (5). Acute coronary syndrome (ACS) is often the first clinical manifestation of CVD (6), occurs due to myocardial blood ischemia by coronary atherosclerotic plaque and includes various types of manifestations like unstable angina (UA) and acute myocardial infarction (STEMI and NSTEMI) (7). A completely blocked coronary artery causes STEMI, while a partially or intermittently occlusion often leads to UA and NSTEMI. All these conditions present with similar signs and symptoms with different intensity (8). Prevalence of young ACS (≤45 years of age) ranged from 2 to 10% among young population (9–11), the frequency of ACS is variable, often overlooked in the young population and creating a significant burden on Pakistan's healthcare system (12). This significant public health issue is the leading cause of death worldwide and research indicates a rising trend of ACS in the younger population, with approximately 38% of patients dying within the same year after experiencing any ACS event, such as UA or an AMI (13,14), similarly trend of ACS in young is rising in Pakistan, almost attributable to various risk factors (15).The ongoing burden of conventional ACS risk factors like diabetes, hypertension, dyslipidemia, obesity, smoking, sedentary lifestyle, family history (8,12), as the increasing burden of these risk factors are major contributors to the development of atherosclerosis and ACS and this relationship has been established through the Framingham Heart Study (16) but in our study setting, the risk factors for young people are not fully understood and continue to be a research concern. Further, the non-conventional ACS risk factors like CRP, creatinine, urea, fibrinogen, blood calcium and others (17,18) are differ among young South Asians and there is a need for further research to gain a deeper understanding of how emerging risk factors contribute to the development of ACS (14).Previous studies suggest to further study to fully determine the risk factors of ACS in young by large sample size and multicenter study to more accurately portray the findings in young and to more generalize the results (14,19). ACS is a growing health issue in young (20), creates death or disability in the prime stage of life causing terrible and catastrophic consequences for a person family, and occupation and also causes the loss of many potential years of life and huge costs on account of health, social, and financial resources (13,14).Despite the rising trend of ACS among young adults, there is a scarcity of comprehensive studies that precisely report ACS risk factors, its manifestations to advance risk assessment and clinical guidelines for young, and predominant older populations data, not precisely reflect the risk factors and manifestation of ACS in young. This breach in knowledge delays the development of targeted prevention and intervention strategies for young adults at risk of ACS. This study is aligned with the United Nations Sustainable Development Goal-3(UNSDGs). A multicenter study with diverse data can help to generalize the results. From the awareness and management prospects, the study promotes lifestyle modification in the young, adds to adopting preventive initiatives and treatment strategies by both the young population and healthcare providers. Last but not least, all these prevent early morbidity and mortality in the young population, which prevents the unanticipated. This study focuses on conventional and non-conventional ACS risk factors, ACS manifestations in young providing a foundation for preventive measures and for improving clinical outcomes in this vulnerable population.

MATERIALS AND METHODS

Study Design and Setting

This Multi Center Cross Sectional Study was conducted from May to October 2024 in three tertiary care hospitals located in different regions of Khyber Pakhtunkhwa, Pakistan, using hospital-based clinical data.

Study-Population

A total of 139 participants with suspected acute coronary syndrome were selected through convenience sampling. The sample size was calculated using OpenEpi with a 10% prevalence estimate and 95% confidence interval.The study used OpenEpi to determine 139 as the required sample size by employing a 5% alpha and a 10% acute coronary syndrome (ACS) prevalence in young people together with a 95% confidence interval. The study participants were chosen by convenience sampling methods.

Ethical Approval:

The University Ethical Committee approved this study under the reference number **IRB/FAHS/Allied-HS/10/24/MS/RS/3518.** Permission to conduct data collection received its approval from every involved hospital. Explanation of the study occurred before participants received either oral or written consent for data collection. The study guaranteed participant confidentiality as well as anonymous participation throughout research progress and after its completion until publication.

Inclusion Criteria:

The survey examined patients between the ages of 20 to 45 who received a diagnosis of acute coronary syndrome either as unstable angina (UA), ST-elevation myocardial infarction (STEMI) or non-ST-elevation myocardial infarction (NSTEMI).The medical research included both male and female patients across the whole participant group.

Exclusion Criteria:

Patients with acute myocardial infarction (MI) or unstable angina due to graft blockage or coronary aneurysm.Individuals with congenital heart diseases.

The study included only patients who were medically fit enough to avoid compromising research results due to their health conditions.

Data Collection and Diagnostic Criteria

The questionnaire used for data collection contained patient history sections together with 12-lead ECG results and cardiac troponin test results to confirm ACS and its subtypes. The researchers obtained demographic statistics together with standard risk factor data from participants. Laboratories within different hospitals processed blood samples to measure C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) together with creatinine, urea, blood glucose and cholesterol levels tests.

ACS Diagnosis Criteria:

- Patients with unstable angina (UA) develop myocardial chest pain together with equivalent symptoms such as dyspnea or epigastric pain or left or right arm pain or jaw or neck pain at rest or during minimal exertion (>20 minutes) that shows ST-segment depression on ECG with normal troponin I values.The fourth universal definition of AMI indicates that Acute Myocardial Infarction (AMI) occurs when patients show myocardial ischemic features (both symptoms and ECG ST changes) together with cardiac troponins surpassing the 99th percentile of the upper reference limit.STEMI: ST-segment elevation >0.1 mV at the J-point in two or more contiguous leads (except V2 and V3). The criteria for ST elevation in V2 and V3 required a standardized reading of 0.2 mV for men who aged 40 years or older and 0.25 mV for men under 40 years and 0.15 mV for women.Medical evidence shows that NSTEMI occurs when ST-segment depression exceeds 1mm in two nearby leads simultaneously with increased cardiac biomarkers.

Left Ventricular Function and Risk Factor Definitions

- Left Ventricular Ejection Fraction (LVEF): Normal (50–70%), mild dysfunction (40–49%), moderate dysfunction (30–39%), and severe dysfunction (<30%).
- The evaluation considered risk factors according to hospital reference ranges together with previously studied literature.CRP >0.5 mg/dL,Urea >50 mg/dL
- Creatinine >1.2 mg/dL,Hemoglobin <14 mg/dL The presence of diabetes is demonstrated by a positive history or FBS >126 mg/dL or RBS >200 mg/dL or patients taking diabetes medications.The patient has hypertension when they either have blood pressure above 140/90 mmHg or require antihypertensive medications for treatment.The condition of dyslipidemia exists when triglycerides measure greater than 200 mg/dL combined with elevated total cholesterol having values above 240 mg/dL along with low-density lipoprotein reading higher than 100 mg/dL and low levels of high-density lipoprotein below 40 mg/dL or patients need lipid-lowering medications. Obesity: Body mass index (BMI) >30 kg/m².Half a decade or longer of continuous cigarette smoking constitutes the condition of smoking. Sedentary lifestyle (lack of exercise).Family history: First-degree relatives with heart disease before 65 years (females) or 55 years (males).

Statistical Analysis

Data were entered and analyzed using SPSS (latest version) and Microsoft Excel. Descriptive statistics included mean and standard deviation (SD) for numerical variables such as cholesterol and CRP. Categorical variables (e.g., ACS types, risk factors) were analyzed using chi-square tests. Multinomial regression was used to assess associations between risk factors and ACS subtypes and age groups. One-way

ANOVA was applied to examine differences in LVEF across ACS subtypes. A p-value <0.05 was considered statistically significant.

RESULTS

Male and female patients were 89 (64%) and female 50 (36%) respectively, the mean age was 39.69±4.405 and the minimum age was 24 years and the maximum age was 45 years respectively. Chest pain was found in the majority 122 (87.8%) (Fig 1) and there was no significant difference (Fisher's Exact Test, p=0.665) between signs/symptoms and gender. Anterior MI found in the majority 38(27%), inferior in 43 (24%), Lateral 19(14%), Extensive anterior 3(2%), anterolateral 17(12%), inferolateral 9(7%), Anterio-inferior 9(7%), anterior and RV in 2(1%) and 8(6%) had no apparent ischemic changes. STEMI was found in the majority 64(46%) (Fig 2) and no statistically significant association (chi-square, p >0.05) between ACS types and gender (male and female). As shown in Figure 3, the age of the research participants was further divided into six groups, the majority of patients 59 (42.4%) were in 36-40 years age range and STEMI being more and statistically no significant association (Fisher exact test, p<0.05) was found among ACS types and age groups. Among the conventional risk factors hypertension was found in the majority 99(71.2%) participants and chest radiation exposure 19(13.7%) and found less. Smoking, dyslipidemia, family history, hypertension, obesity, and lack of exercise were more in STEMI while diabetes and chest radiation exposure history patients were more likely to have NSTEMI, a statistically significant association (chi-square, p<0.05) found between ACS manifestation with diabetes and hypertension only (Table 1).

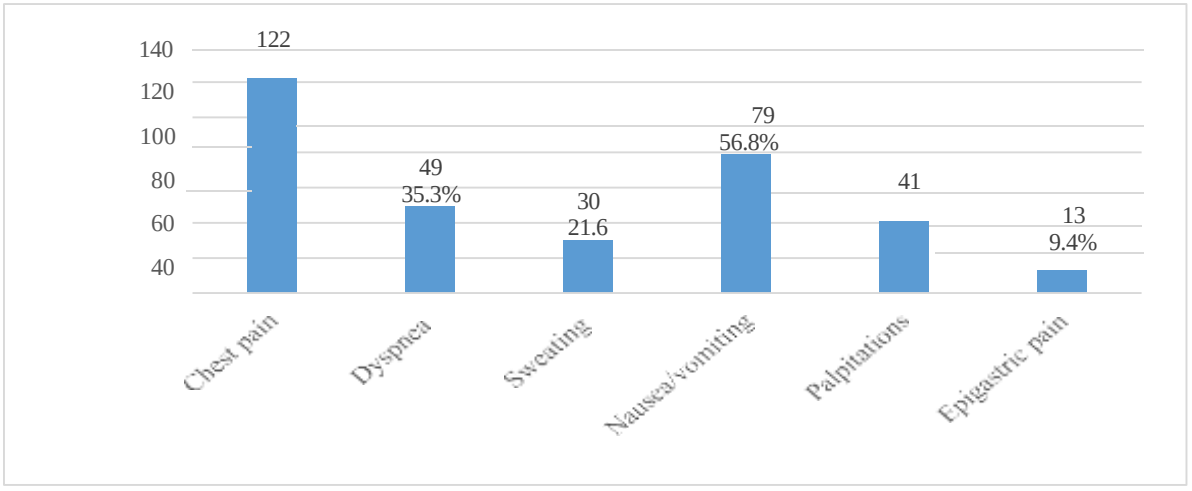

Fig 1: Signs and symptoms of acute coronary syndrome in young (n=139)

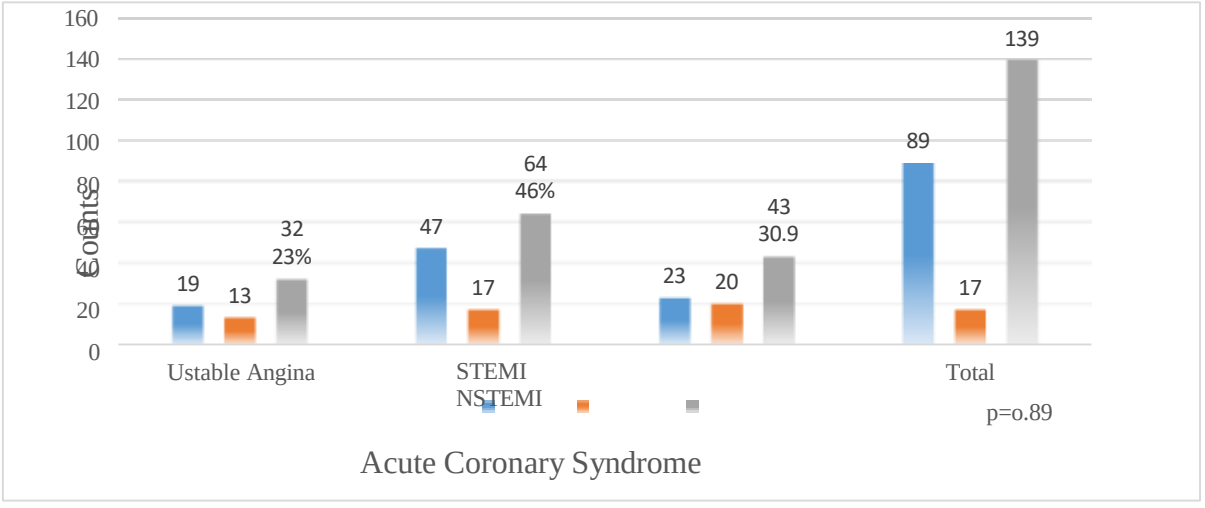

Fig 2: Comparison of acute coronary syndrome manifestation among gender (n=139)

Among gender (male=89 and female=50) almost all risk factors were found more in males vs female as smoking in 44 (89.8%) vs 5(10.2%), diabetes 28(54.9%) vs 23(45.1%),yslipidemia 47(66.2%) vs 24(33.8%), family history 58(63.0%) vs 34(37.0%), hypertension60(60.0%) vs 39(39.4%), obesity 35(57.4%) vs 26(42.6%), lack of exercise 40(59.7%) vs 27(40.3%), chest radiation exposure 8(42.1%) vs 11(57.9%), smoking was the most prevalent risk factor among males 44(89.8%), and chest radiation was most prevalent in females 11 (57.9%), a significant association (chi-square, $p<0.05$) was found among gender with smoking and chest radiation exposures only.Risk factors were more prevalent in the 36-40 years age group except diabetes and chest radiation exposure were more found in 41-45 years age group, significant association (Fisher exact test, $p <0.05$) found between age groups and chest radiation only (Table 3).Among different types of ACS, patients with unstable angina exhibited higher mean levels of SYS-BP, DBP, BMI, and creatinine. In contrast, patients with STEMI had higher mean levels of HbA1c, urea, total cholesterol, triglycerides, LDL, and troponin-I. While, participants with NSTEMI showed higher mean levels of fasting blood sugar, random blood sugar, C-reactive protein CRP, and ESR. Additionally, mean levels of HDL were lower in STEMI patients, mean HB was lower in UA patients, and mean ejection fraction (EF%) was lower in NSTEMI patients respectively (Table 4).

Table 1: Comparison of ACS manifestation and conventional risk factors (n=139)

Risk Factors		Acute Coronary Syndrome Manifestations				P value
		Unstable angina n=32	STEMI n=64	NSTEMI n=43	Total	
Smoking	Yes	11 (22.4%)	24 (49.0%)	14 (28.6%)	49 (100.0%)	0.865
Diabetes	Yes	13 (25.5%)	13 (25.5%)	25 (49.0%)	51 (100.0%)	0.000
Dyslipidemia	Yes	14 (19.7%)	33 (46.5%)	24 (33.8%)	71 (100.0%)	0.583
Family History	Yes	21 (22.8%)	45 (48.9%)	26 (28.3%)	92 (100.0%)	0.577
Hypertension	Yes	26 (26.3%)	38 (38.4%)	35 (35.4%)	99 (100.0%)	0.017
Obesity	Yes	17 (27.9%)	25 (41.0%)	19 (31.1%)	61 (100.0%)	0.424
Lack of Exercise	Yes	17 (25.4%)	34 (50.7%)	16 (23.9%)	67 (100.0%)	0.222
Chest Radiation Exposure	Yes	2 (10.5%)	8 (42.1%)	9 (47.4%)	19 (100.0%)	0.189

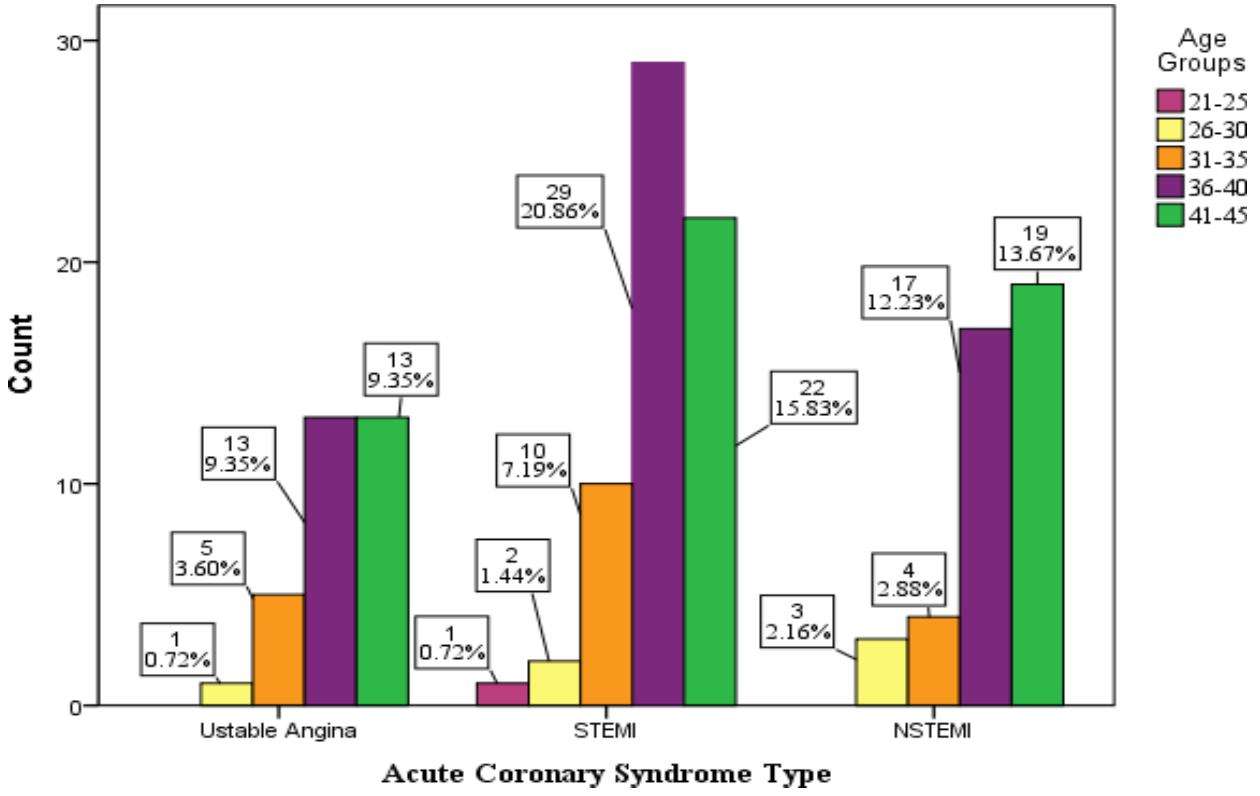

Fig 3: Comparison of acute coronary syndrome type among age groups

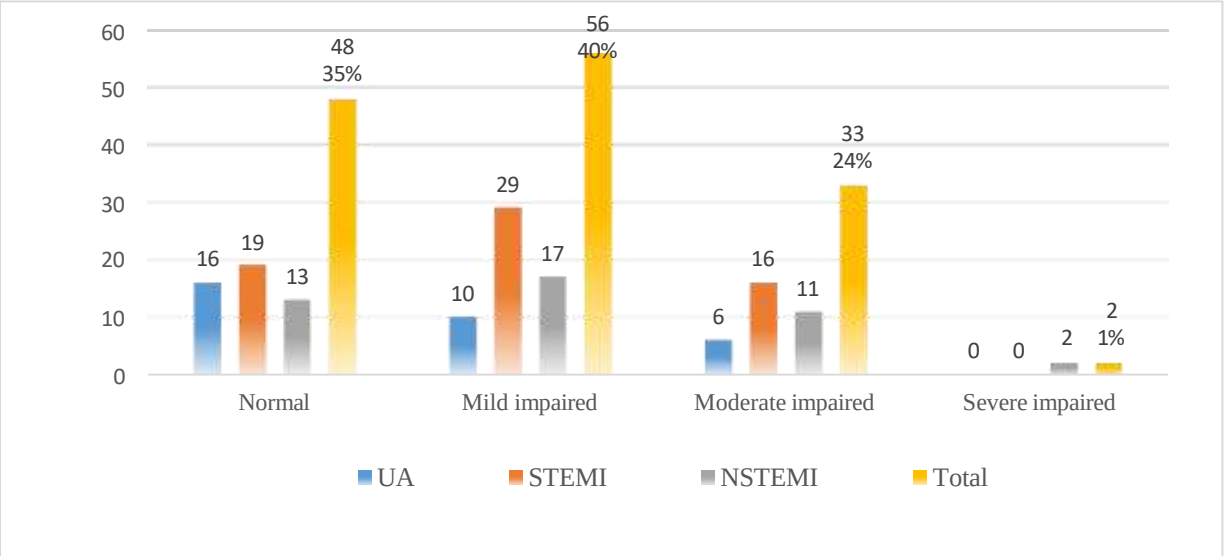

Fig 4: Comparison of systolic function in ACS types (n=139)

Table 2: Continuous variables in research participants (n=139)

Variables	Mean	Std. Dev	Mini	Max
Height (m)	1.6	0.9	1.4	1.87
Weight (kg)	81.7	13.0	50	130
SYS BP (mmHG)	140.5	21.1	80.0	190.0
DIA BP (mmHG)	87.9	11.9	50.0	110.0
BMI (kg/m^2)	30.9	5.5	46.5	20.8
FBS (mg/dl)	101.8	42.7	9.2	378.0
RBS (mg/dl)	181.1	91.4	8.9	538.0
HBA1c (%)	7.9	6.0	4.2	53.0
CRP (mg/dl)	7.3	11.4	0.1	81.0
ESR (mm/hr)	22.3	16.3	0.2	140.0
Urea (mg/dl)	39.7	20.1	0.7	140.0
Creatinine (mg/dl)	1.1	0.5	0.4	6.87
TC (mg/dl)	212.1	66.7	18.0	425.0
TG (mg/dl)	221.4	140.2	49.0	1062.0
HDL (mg/dl)	42.16	10.8	23.0	88.0
LDL (mg/dl)	144.1	45.7	13.6	298.0
HB (mg/dl)	13.7	2.03	7.71	18.5
EF (%)	48.1	9.5	25.0	68.0

Table 3: Comparison of ACS risk factors among age groups (n=139)

Risk Factors		Age groups (years) 21-25 n=1	26-30 n=6	31-35 n=19	36-40 n=59	41-45 n=54	P value
Smoking	Yes	0 (0.0%)	1 (2.0%)	4 (8.2%)	25 (51.0%)	19 (38.8%)	0.382
Diabetes	Yes	0 (0.0%)	1 (2.0%)	4 (7.8%)	20 (39.2%)	26 (51.0%)	0.133
Dyslipidemia	Yes	0 (0.0%)	2 (2.8%)	8 (11.3%)	31 (43.7%)	30 (42.3%)	0.612
Family History	Yes	1 (1.1%)	5 (5.4%)	14 (15.2%)	44 (47.8%)	28 (30.4%)	0.062
Hypertension	Yes	0 (0.0%)	6 (6.1%)	13 (13.1%)	40 (40.4%)	40 (40.4%)	0.264
Obesity	Yes	0 (0.0%)	2 (3.3%)	11 (18.0%)	26 (42.6%)	22 (36.1%)	0.594
Lack of Exercise	Yes	0 (0.0%)	2 (3.0%)	9 (13.4%)	33 (49.3%)	23 (34.3%)	0.481
Chest Radiation Exposure	Yes	0 (0.0%)	2 (10.5%)	0 (0.0%)	5 (26.3%)	12 (63.2%)	0.025

Table 4: Descriptive comparison of risk continuous variables among ACS types (n=139)

Variables	Unstable Angina n=32		STEMI n=64		NSTEMIs n=43	
	Mean	Std. Dev	Mean	Std. Dev	Mean	Std. Dev
SYS BP	146.25	19.92	136.04	21.35	142.79	20.56
DIA BP	90.53	11.28	86.09	12.84	88.48	10.77
BMI	31.03	4.58	30.68	5.86	30.91	5.76
FBS	94.62	22.48	91.69	30.25	122.11	60.22
RBS	153.12	69.01	164.34	69.23	226.97	116.35
HBA1c (%)	6.78	1.97	8.54	9.83	8.03	2.43
CRP	4.46	4.54	7.08	10.04	9.83	15.75
ESR	16.71	6.71	22.15	14.44	26.56	22.01
Urea	37.30	21.30	42.57	22.40	37.18	14.66
Creatinine	1.17	1.08	1.10	0.45	1.03	0.49
T. Cholesterol	196.93	55.92	220.67	70.76	210.72	67.19
Triglycerides	193.93	72.92	245.09	190.40	206.65	68.19
HDL	44.34	12.51	41.42	8.46	41.62	12.36
LDL	128.46	40.85	152.24	45.27	143.76	47.48
HB	13.28	2.41	13.98	1.85	13.48	1.95
EF (%)	51.84	9.77	47.69	8.19	46.54	9.50

Upon applying multinomial logistic regression, among STEMI respondents, ESR and urea significantly impact ACS manifestations. As ESR and urea increased by one unit the odd ratio/probability of STEMI as compared to UA respondents was more by 1.092 and 1.055 times respectively. Among NSTEMI respondents RBS and ESR have a significant impact ($p<0.05$) on ACS manifestations. As RBS and ESR increased by one unit the odd ratio/probability of NSTEMI as compared to UA respondent was more by 1.013 and 1.104 times respectively. other variables as mentioned in Table 4 among STEMI and NSTEMI relative to UA were statistically not significant. Pulmonary artery pressure was found normal in the majority 77 (55.4%) of ACS patients, mild pulmonary hypertension in 45(32.4%), moderate in 15(10.8%), and severe PAH in 2(1.4%) patients. Severe PAH was in 1(1.6%) STEMI and NSTEMI patients each, moderate and mild PAH was found in the majority of STEMI in 10(15.6%) and 20(44.4%) patients respectively, and no statistically significant association (Fisher's Exact test, $p >0.05$) found inpulmonary artery pressure and different types of ACS.The majority 16(25.0%) of patients having moderate and mild impaired LV systolic dysfunction 29(45.3%) had STEMI (Fig 4). Ef was significantly different among the three ACS groups $F (2, 136)=3.189$, $p <0.05$. Post hoc test reveals significant differences

among ACS type with UA (M=51.84, SD=9.77), STEMI (M=47.69, SD=8.19), and STEMI (M=46.54, SD=9.50), and significant difference found (p=0.043) between UA and NSTEMI and the finding shows EF(%) was lower in NSTEMI patients.

DISCUSSION

The prevalence of ACS risk factors are increasing at young age (24), also sudden cardiac arrest in young is significant after ACS and a study shows half (15%) of deaths due to sudden cardiac arrest among all ACS deaths (30%) (25), nevertheless, ACS progression can be prevented upon early recognition of ACS risk factors (26).In this study, the mean age was 39.69±4.405, a little higher than results of Siddiqui *et al.,* 35.80±4.21 years as but similar to this study majority of patients (62.4%) were in the age group 36-39 years (19) Same as this study Yılmaz & Cosansu and Khan *et al.,* show mean age of 40.5±4.5 and 39±6 among young (11,14), in contrast, Revaiah *et al.*, report a mean age of 35.5 ± 4.7years, this lower may be due to the study on young less than 40 years of age (22) and also by Bush *et al.* on the mean age of young 36±4.69 years lower than this study may be due to less sample size (27). In this study, 89(64%) were male and 50(36%) were female, nearly close to the 30 (60%) male and 20(40%) female by Ahamed *et al.* (28). Same to this in Revaiah *et al.* in which males 175(96.2%) and females 7(3.8%) being the male in majority (22), and also reported 289(89.8%) young male by Chen *et al.* (29)In contrast, Siddiqui *et al.* reported a higher 72(85%) male and 13(15%) female (19) and in another study, male were 86(71.66%) and female 34(28.33%) (30) but similarly male were in the majority.Chest pain 122(87.8%) was more prevalent in this study, which aligns with the findings of Chen *et al.*, where chest pain was identified in the majority of younger patients (307 cases, 97.5%)(29). Revaiah *et al.,* in young patients (age≤40 years) also found chest pain in the majority 180(98.9%), atypical chest pain 1(0.5%), and dyspnea 9(4.9%) higher than our results (22), and in Bush *et al.*, similar to this study, angina was in 33(68.8%), atypical angina 13(27.1%), dyspnea 10(20.8%) higher comparative to this study, PND in 4(8.3%) and orthopnea in 3(6.3%) patients respectively (27), Ahamed *et al.,* shows chest pain 46(92%), breathlessness 20(40%), arm pain 8(16%), jaw pain 5(10%), and syncope 0(0%) (28) respectively as similar to this study. We found UA in 32(23%), STEMI in 64(46%), and NSTEMI in 43(30.9%) patients, nearly close to the findings as UA in 164(18.5%), STEMI 486(54.8%), NSTEMI 237(26.7%) by Yılmaz & Cosansu (11), the difference may be due to a higher sample size and retrospective design, Ali *et al.*, show UA in 17.5%, STEMI 73.4%, and NSTEMI in 9.2% of participants respectively (13). Our study result was also in near agreement with Kassam *et al* in which STEMI was found I n 77(57.5%) with little difference due 50 years young age participants (31). Peerwani *et al.* reported UA 422 (14.6%),STEMI 1302 (45.0%) and NSTEMI 1170 (40.4%)in your, and similar to this study STEMI found in the majority (32).In this study anterior MI was found in the majority 38(27%), inferior in 34(24%) same to results of another in which AWMI 52(43.3%), IWMI 32(26.66%), PWMI 11(9.16%) reported in young (30). Another study in age ≤40 years, shows that STEMI 149(82%) and AWMI 105(58%) in the majority, same to this study IWMI was in 41 (23%), and LWMI 3 (1%) respectively (22), Nearly similar to this study a study reports 51(68.9%) AWMI, and 23(31.1%) IWMI among young STEMI (15). Ahamed *et al.* show anterior wall MI in 29(58%), posterior wall MI in 15(30%), and global in 6(12%) respectively (28). Ahmad *et al.* inferior wall MI was common (37.2% cases) among young STEMI patients and AWMI among NSTEMI (33) with the difference to our results which may be due to UA exclusion in the previous study.In this study mean systolic/diastolic BP was 140.48±21.08/87.86±11.94 and hypertension was found in 99(71.2%) participants with significant difference (p>0.05) among types ACS, similar to the result reported by Kassam *et al* (31), nearly close findings reported by another study as mean systolic/diastolic BP (mmHg) was 135.6±23.3/86.4±15 and hypertension in 140 (41.8%) (14), also close to this study hypertension in 77.6% of participants found by Vazquez *et al* (34). Lower than this study Sun *et al.*, (18–35 years of age) show, hypertension in 402 (48.55%) and SBP/DBP of 126.04 ± 16.01/77.71 ± 13.26 respectively (35) the difference may be due to lower age, Another study shows hypertension in 125 (38.8%) among 322 (16.2%) young (≤50 years age) and close to this study mean SBP was 130 mmHg (29).Diabetes was found in 51(36.7%) with significant difference (p<0.05) among ACS types, mean FBS was 101.78±2.70 and RBS was 181.14±91.36, HBA1c 7.98±6.88 in this study lower than other studies result reported as diabetes mellitus in 70(20.9%) by Khan *et al* (14), in 10(11.8%) (19), in 24(20%) by Iragavarapu *et al* (30) and in 15.9% of participants as reported by another study on young (22), and this difference may be due to sample size and different study designs. DM in 196(22.1%) with mean RBS 147±86 and similar to this study mean HBA1c was 7±2.4 reported by Yilmaz *et al.* (11), another study reported DM in 162(19.57%) with mean HbA1c 5.6(5.2–6.2%) among 828 young (18-35 years) ACS patients (35), contrary significant difference in DM among genders reported by Siddiqui *et al.* (19).Smoking is an independent predictor of ACS in young (35), compared to this study result of 49(35.3%) smoking, higher finding of 140(41.8%) smoking shown by another study (14) and 36(44.4%) smokers in young (20-35 years) (15), and in 732(82.5%) participants as reported by another study on young (11). Revaiah *et al.*, have shown smoking as a prevalent risk factor (56%) (22) and Bush *et al.*, reported smoking in 31 (64.6%) young participants (27), the difference may be due to the study on age <40 years. Another study shows a higher number of current smoking among young (≤50 years) in 201(62.8%) vs 564(34.1%) in old

with a significant difference (p<0.001) (29), and also reported tobacco consumption in 30(60%) of research participants by Ahamed *et al.* (28), the findings of this study are close to other studies results as reported smoking in 31(36.5%) participant (19), in 31(25.8%) (30), and 36(44.4%) participants by Khan *et al.* among 20- 35 years age participants (15) moreover, we found smoking in only 5(10.2%) of females, this low number may be due to fear of expressing, considered social evil due to cultural and Islamic beliefs as well.Family history is also an independent risk factor for ACS in young (35), in this study 92(66.2%) participants had a family history, close to the 70(52.2%) findings of Kassam *et al.*, among young ACS (31), and higher than the results of 30(9%) (14) and 8(9.9%) participants (15) reported by other studies. Near to close to our findings 45(52.9%) positive family history participants, which also reported a significant difference in family history among gender (19). Other studies show positive family history as: 18.2% (22), 26(30%) (30), in 15(31.3%) young participants respectively (27).Dyslipidemia increases the risk of ACS and in this study 71(51.1%) participants had dyslipidemia which was higher than the results 31(9.3%) and 13(15.3%) participants (14,19), and 21 (17.5%) by Iragavarapu *et al.* (30), and lower than the findings of Yılmaz *et al.*, in which 681(76.8%) participants had dyslipidemia (11) and these differences may be due to lifestyle and genetic variation among the different populations. Another study on young shows mean TC 197.96±43.57, LDL 141.53±40.27.HDL 42.48±12.81, triglycerides 177.19±52.9 (27). Our findings mean(mg/dl) TC 212.13±66.71, HDL 42.16±10.76, LDL 144.15±45.66, and TG 221.42 ± 140.22 were closer to the findings of another study in which triglyceride (mg/dL) 235±228, HDL-C (mg/dL) 38±9, LDL-C (mg/dL) 144±45 reported respectively (11), and in another study among 1982 young ACS, hypercholesterolemia found in 105(36.2%), Triglycerides (mmol/L) 1.92, Total cholesterol (mmol/L) 4.74, HDL-C (mmol/L) 1.06, LDL-C (mmol/L) 2.98 and concluded prevalence hypercholesterolemia higher in younger compared with the older group with significant difference (29).Obesity is a major contributor to building ACS and was present in 61(43.9%) participants in this study while 52(37.4%) were overweight and Mean BMI was 30.83±5.52 respectively. similar findings (41.5%) were also reported by Ali *et al* (13), higher obesity found in another study in which the mean BMI (kg/m2) was 27.4±3.7, 2 (0.6%), overweight found in 211 (63%) and obesity in 57 (17%) participants respectively (14). Close to our results different studies reported a mean BMI (kg/m2) of 28.5±4, overweight in 246(27.7%), obesity in 57(17.7%) in young ACS (11), mean BMI 27.13±7.5kg/m^2 and 14(16.5%) obesity (19), and BMI (kg/m2) 26.8±5.4 and obesity in 18 (15%) (30), another study in a young group of ACS (20- 35 years) participants shows a mean BMI 26.76±2.85 kg/m2, obesity in 13.6% of participants, overweight in 67.9%, 1(1.2%) was underweight while 14(17.3%) had normal BMI (15) respectively. In this study mean LVEF% was 48.29±9.50, with mild LV systolic dysfunction common, similar to the mean LVEF 46.0±12.4 reported by Kassam *et al* (31). A study reported LV systolic dysfunction as Mild in 28(23.33%), Moderate in 43(35.83%), and severe in 10(8.3%) ACS patients (30). LVEF was significantly lower in young ACS patients compared to non-CAD subjects in a study (34), close to our finding mean LVEF% of 46.5±9.9 reported by a study on young ACS participants (11).The non-conventional ACS risk factors like CRP, creatinine, urea, blood calcium, low HB, and radiation exposure history also play a role in building ACS (17,18), a case-control study by Afsar *et al.* has shown in control vs ACS groups: urea 28.65±7.40 vs 46.97±27.18 (p=0.000),creatinine 0.80±0.13 vs 1.15±0.59 (p=0.000),ESR 15.37±9.77 vs 20.99±20.63 (p=0.026),calcium 9.60±0.37 vs 9.26±0.45 (p=0.000), a significantly higher level (p<0.001) of creatinine and ESR in ACS than the control group (18), this shows the association of creatinine and ESR with ACS .Mean creatinine (mg/dl) of 0.91±0.22 reported by Vazquez *et al.* (32) and a retrospective study on young ACS reports higher mean CRP (mg/L) 8.9±13.5 and lower creatinine 0.97±0.94 than this study (11), another retrospective 1:1 case-control (415 each) on a young female (≤44 years) shown ACS vs control as: high CRP in 31(7.47%) vs 4 (0.96%) (p=0.000) with a mean (3.40±5.98 vs 1.24±1.46 p 0.000 mg/L), HB(g/L)127.85±15.20 vs 129.39±12.10 (p=0.107), serum creatinine(umol/L) 63.40±19.32 vs 59.22±11.12 (p=0.000), and further reports LDL, TG, creatinine, and CRP in the ACS group were significantly higher (P <0.01) than in the control group (23).A multicentered study reports mean creatinine (µmol/L) of 72.10 in young (29), and another study shows high-sensitive C-reactive protein 29.52±30.42 (27) and a single-center observational study on 828 young (18–35 years of age) ACS patients reports, mean BUN (4.94±1.39 mmol/L), hyperuricemia in 367 (44.32%), mean creatinine (74.68±15.14) found in young ACS patients and raised mean CRP 3.11(1.09–11.40mg/L) in ACS compared non-ACS patients respectively(34).

CONCLUSIONS

ACS prevalence in young is rising in Pakistan. Chest pain, nausea/vomiting, anterior and inferior MI were common. STEMI was found in the majority. Hypertension, family history and dyslipidemia were the prevalent risk factors while smoking and radiation exposure showed significant association with gender and chest radiation exposure history with age groups. Mean SYS & DIA BP, BMI, creatinine, HDL, and EF were higher in UA, mean HBA1c, urea, TC, Triglyceride, LDL, and HB were higher in STEMI while mean RBS and FBS, CRP, and ESR were higher among NSTEMI patient. ESR and Urea were significantly

higher in STEMI compared to UA while RBS and ESR were significantly higher among NSTEMI compared to UA both with positive odd ratios. Mild PAH and mild impaired systolic function were commonly found and EF (%) was significantly different among ACS types.

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STUDY STRENGTH

Multicenter data: Diverse data obtained with increased generalizability of results over young.
Sample Size: The sample size was equally divided into three tertiary care hospital
Advanced Equipment: The study utilized the latest model of ECG, Echocardiography machine, and others, ensuring accurate results.

Limitations of the Study

Only case group: The study includes only ACS cases. Control groups help in the exact determination of differences and association of risk factors with ACS.

Recommendations

Cohort or case-control studies with large samples are recommended to gain a deeper understanding of the association of risk factors among young individuals.

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AUTHORS CONTRIBUTION

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