Original Research Article

Acute Coronary Syndrome in Egyptian Women During Their Reproductive Age Period

Abstract

Background: Young women have low risk of acute coronary syndrome (ACS) during their reproductive period, mainly due to the physiologically protective effect of estrogen hormone on the coronary endothelium. The purpose of this study was to assess the risk factors of ACS in the Egyptian women patients during their reproductive age period, who admitted to Tanta University Cardiovascular department hospital.

Results: Obesity, hypertension, diabetes mellitus, chronic kidney disease, systemic lupus erythematosus, myocardial bridge, cushion syndrome and radiotherapy for breast cancer were significantly independently ACS risk factors that correlated to the SYNTAX score. There is significance of coefficient of the independent variable in the risk factors (Group A, group B, group C separately and groups A, B, C together) on the severity and level of SYNTAX score in ACS. The regression analysis was significant in groups A and B of ACS risk factors separately. While the regression analysis was significant and there was a clear relationship between ACS risk factors- groups A, B, C. together and SYNTAX score.

Conclusions: There was a positive relationship between the increase total number of ACS risk factors subgroups (Traditional, Nontraditional and Gynecological) and the severity of coronary artery stenosis that assessed by SYNTAX scorer.

Keywords: Acute Coronary Syndrome, Egyptian women, Reproductive Age Period, Gynecological risk factors.

Background:

The acute coronary syndrome (ACS) can be considered as the main cause of morbidity and mortality worldwide, its incidence rate is recently increased especially in the developing countries, about 3% to 10% of acute coronary syndrome occurred in young individual either male or female who aged below 45 years [1]. The atherosclerotic cardiovascular disease risk score (ASCVD) increases usually with increase age so, the ischemic heart disease usually delayed in women than men duo to the impact of hormonal sex difference during the fertile period of life [2]. While female are more likely to suffer from coronary heart disease than breast cancer throughout their lives [3].

Young women have low risk of coronary heart disease as a general and (ACS) during their reproductive period and until reach the age of menopause mainly due to the hormonal protection specially estrogen, as this hormone reduces cellular hypertrophy, increases vessels wall elasticity and stimulate antioxidants and anti-inflammatory products on the coronary vessels, also estrogen hormone play an important role against coronary stenosis through stimulate endothelial cells nitric oxide production. So, atypical ischemic symptoms and the low awareness of the coronary artery disease risk factors among women in this age can lead to missed diagnosis of ischemic heart disease [4].

The Women′s Ischemic Syndrome Evaluation (WISE) study, suggests that: if a central ovarian function disorder occurred, it may leads to premenopausal estrogen deficiency and that play a role as a potent ischemic heart disease risk factor, also recurrent and prolonged psychic stress can leads to central disorder in the ovulatory cycle which also leads to decrease serum estrogen hormone level and that increase the risk of obstructive coronary artery disease in women who suspected ischemia[5].

It is noted that, women with (ACS) are more likely to have thrombus formation, plaque erosion and microvascular coronary dysfunction while men usually have significant

obstructive coronary artery disease [6]. The major cardiovascular risk factors can be classified into three main groups: Traditional risk factors including: familial dyslipidemia, diabetes mellitus, obesity and metabolic syndrome, hypertension, chronic kidney disease and smoking. Non-traditional risk factors including endocrinal hormonal disorder (mainly thyroid and suprarenal glands disorder), auto-immune and vascular disease, migraine, coagulation disorders, stress lifestyle (which was assessed by Holmes and Rahe stress scale) and depression, anemia, myocardial bridge and some viral disease. Gynecological risk factors including: preeclampsia and/or eclampsia, gestational diabetes, polycystic ovary syndrome, primary ovarian dysfunction and post premature menopause hormonal treatment, hysterectomy and/or oophorectomy, endometriosis, vitamin D deficiency, contraceptive methods, chemotherapy and radiotherapy of Brest cancer and in vitro fertilization hormonal treatment [6].

The aim of this study was to assess the risk factors of acute coronary syndrome (ACS) in the Egyptian women patients during their reproductive age period, who admitted to Tanta University Cardiovascular department hospital.

Methods:

The aim of this study was to assess the risk factors of ACS in the Egyptian women patients during their reproductive age period, who admitted to Tanta University Cardiovascular department hospital.

Study design and population: This a retrospective study was carried out on 300 female patients aged above 18 years till the age of menopause who presented with acute coronary syndrome (ACS) either unstable angina (UA), ST elevated myocardial infarction (STEMI), or non-ST elevated myocardial infarction (Non-STEMI) at Cardiology Department, Tanta University Hospital.

Excluded criteria: female patients before puberty, post-menopausal patients with acute coronary syndrome, female patients with heart failure, cardiomyopathy and post CABG (coronary artery bypass graft surgery), patients with moderate to severe valvular heart disease, the positive history of aortic dissection, decompensated liver cell failure and the severe anemic patients (hemoglobin level was less than 8 g/dl).

All patients were subjected to full medical history, detailed clinical examination, cardiac biomarkers (Troponin I and T, Creatine Kinase MB (CK-MB)), standard supine 12 leads electrocardiography, echocardiography study, essential and special laboratory investigations according to each patient was needed (as thyroid function test, cortisol level test, hepatitis C-virus antibody and hepatitis B-surface antigen) and coronary angiography, identify the common risk factors according to its main subgroups: (Traditional, nontraditional and gynecological risk factors) and identify the relation between the acute coronary syndrome risk factors groups and the SYNTAX score level.

Statistical analysis

All data were analyzed using SPSS 22.0 for windows (SPSS Inc., Chicago, IL, USA). Normality was tested using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test (χ^2) and Fisher exact were used to calculate difference between qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation) for parametric and median and range for non-parametric data. One way ANOVA test supplemented with LSD post hoc test was used to compare between more than two dependent groups of normally distributed variables. While Kruskal-Wallis test was used for non-normally distributed variables. All statistical comparisons were two tailed with significance Level of P-value ≤ 0.05 indicates significant.

Results:

Patients' distribution according to their social status, employing status, children status, age, BMI, obesity grades, ACS- types. **Table 1**

Table 1: Patients' distribution according to their social status, employing status, children status, age, BMI, obesity grades, ACS- types

Social Status	**No. (%)**
Single	42 (14.0 %)
Married	192 (64.0 %)
Widow	34 (11.3 %)
Divorced	32 (10.7 %)
Employing Status:	
Worker	170 (56.7 %)
Housewives	130 (43.3 %)
Children Status:	
Have children	230 (76.7 %)
Have no children	70 (23.3 %)
Age categories	
≤ 25	10 (3.3%)
26 - 30	30 (10.0 %)
31 - 35	30 (10.0 %)
36 - 40	42 (14.0 %)
41 - 45	72 (24.0 %)
46 - 50	116 (38.7 %)
BMI- categories	
Normal	2(0.6%)
Pre-obese (overweight)	44(14.7 %)
Obesity Grades	

Obese class 1	120 (40.0 %)
Obese class 2	102 (34.0 %)
Obese class 3	32 (10.7 %)
ACS- types	
U.A.	152(50.7 %)
STEMI	42(14.0 %)
Non-STEMI	106(35.3 %)

Data are presented as frequency (%). U. A: Unstable angina, STEMI: ST elevated myocardial infarction, Non-STEMI: Non-ST elevated myocardial infarction.

Table 2 shows the relationship between ACS subtypes and its management methods, the site and percentage of coronary artery lesions in unstable angina UA, ST segment elevation and non-ST segment elevation myocardial infarction. LAD had the upper hand of lesion sites (It formed 66.7% of significant STEMI lesions and formed 64.2% of significant non-STEMI lesions). The second common site was the RCA (It formed 47.6% of significant STEMI lesions and formed 37.7% of significant non-STEMI lesions). The third common site was the LCX (It formed 42.9% of significant STEMI lesions and formed 34.0% of significant non-STEMI lesions). The fourth common site was the LM. With nearly equal presentation in STEMI and Non-STEMI (28%). **Table 2**

Table 2: Relationship between acute coronary syndrome subtypes and its management methods, the site and percentage of coronary artery lesions in ST segment elevation and non-ST segment elevation myocardial infarction.

ACS – types:	**U.A.** **No. 152**	**STEMI** **42**	**Non-STEMI** **106**
Methods of Management	**No.%**	**No.%**	**No. %**
Medical treatment and/or thrombolytic	124 (81.6)	4 (9.52%)	2 (1.9%)

PCI			
L.M	0	2 (4.76%)	4 (3.8%)
LAD	10 (6.6%)	6 (14.28%)	22 (20.8%)
RCA	12 (7.9%)	6 (14.28%)	20 (18.9%)
LCX	6 (3.9%)		10 (9.4%)
L.M & LAD		4 (9.52%)	8 (7.5%)
LAD & RCA		2 (4.76%)	10 (9.4%)
LAD & LCX		6 (14.28%)	8(7.5%)
RCA & LCX		2 (4.76%)	2 (1.9%)
L.M & LAD & RCA			4 (3.8%)
L.M & LAD & LCX			12 (11.3%)
LAD & RCA & LCX		4 (9.52%)	2 (1.9%)
L.M & LAD & RCA & LCX		6 (14.28%)	2 (1.9%)
Site and percentage of coronary artery lesions			
LAD	10 (6.6 %)	28 (66.7 %)	68(64.2 %)
RCA	12 (7.9 %)	20(47.6 %)	40(37.7 %)
LCX	6 (3.9 %)	18(42.9 %)	36(34.0 %)
L.M.		12(28.6 %)	30(28.3 %)
Medical treatment and/or thrombolytic	124 (81.6 %)	4(9.5 %)	2(1.9 %)

Data are presented as frequency (%). U. A: Unstable angina, STEMI: ST elevated myocardial infarction, Non-STEMI: Non-ST elevated myocardial infarction PCI: percutaneous coronary stent implantation, LM: left main coronary artery, LAD: left anterior descending coronary artery, RCA: right coronary artery, LCX: left circumflex coronary artery.

Obesity was the 1st level of risk factors in ACS (it formed 84.7% of the sample. Hypertension was the 2nd level of risk factors in ACS (it found in about 61.3%). Stress lifestyle was the 3rd level of risk factors in ACS (it formed 32.7%). **Figure 1**

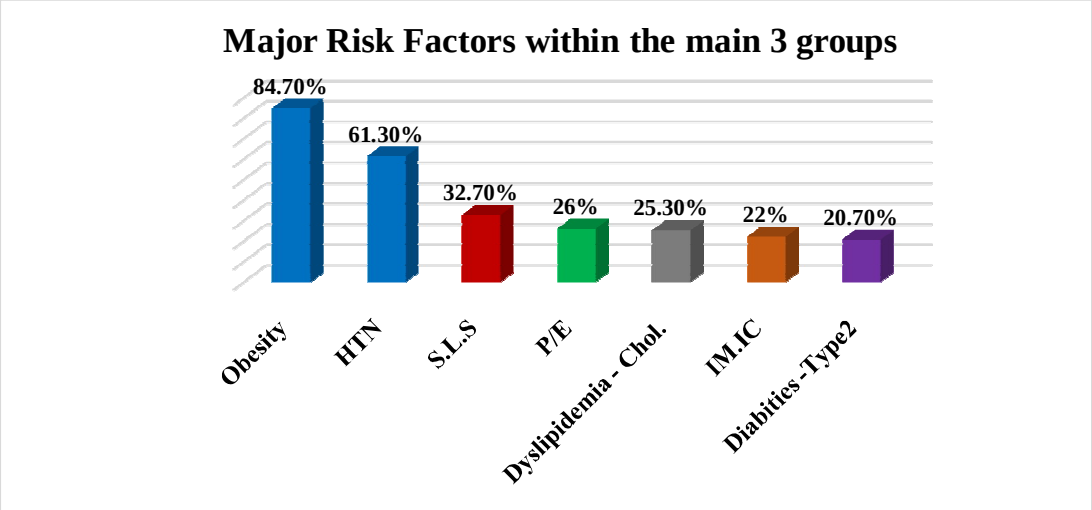


Figure 1: The percentage of major risk factors of acute coronary syndrome

The main four Traditional risk factors other than obesity that effected on unstable angina: Hypertension 57.9%, Hypercholesterolemia 26.3%, Hypothyroidism 23.7%, Type 2 diabetes mellitus 22.4%, The main four Traditional risk factors other than obesity that effected on STEMI: Hypertension 72.4%, Both total Dyslipidaemia & type 1 - diabetes mellitus 33.3%, Both Smoking & Chronic kidney disease 28.6%. The main four Traditional risk factors other than obesity that effect on Non- STEMI: Hypertension 60.4%, Hypercholesterolemia 30.2% , Type 2 Diabetes mellitus 22.6%, Type 1 Diabetes mellitus 20.8%, Obesity (after excluding the overweight patients), affected 254 patients (84.7%) Obesity grades distribution in ACS, about 47.4% of U.A. patients & 37.7% of non-STEMI patients in this study were considered Class 1 Obesity, While 47.6% STEMI patients was considered Class 2 Obesity, The highest class 3 obesity distribution was found in STEMI group & formed 23.8% of the sample. **Table 3**

Table 3: Traditional risk factors, obesity grades and BMI Classification of unstable angina, ST segment elevation and non-ST segment elevation myocardial infarction.

	U. A No. (%)	STEMI No. (%)	Non-STEMI No. (%)

Traditional risk factors			
TG.	6 (3.9 %)	2 (4.8 %)	18(17.0 %)
Cholesterol.	40(26.3 %)	4(9.5 %)	32(30.2 %)
TG. & chol.	24(15.8 %)	14(33.3 %)	6(5.7 %)
Hypertension	88(57.9 %)	30(72.4 %)	64(60.4 %)
DM – Type 1	22(14.5 %)	14(33.3 %)	22(20.8 %)
DM – Type 2	34(22.4 %)	4(9.5 %)	24(22.6 %)
CKD	12(7.9 %)	12(28.6 %)	20(18.9 %)
Hyper Thyroidism	10(6.6 %)	2(4.8 %)	6(5.7 %)
Hypo Thyroidism	36(23.7 %)	2(4.8 %)	4(3.8 %)
Smoking	16(10.5 %)	12(28.6 %)	18(17.0 %)
Obesity grades **BMI Classification**			
Overweight	18 (11.8 %)	4 (9.5 %)	22 (20.8 %)
Obese class 1	72 (47.4 %)	8 (19.0 %)	40 (37.7 %)
Obese class 2	46 (30.3 %)	20 (47.6 %)	36 (34.0 %)
Obese class 3	16(10.5 %)	10 (23.8 %)	6 (5.7 %)

Data are presented as frequency (%). U. A: Unstable angina, STEMI: ST elevated myocardial infarction, Non-STEMI: Non-ST elevated myocardial infarction, TG. & Chol.: hypertriglyceridemia and hypercholesterolemia, DM: diabetes mellitus, CKD: chronic kidney disease, BMI: body mass index

In unstable angina Stress lifestyle. (35.5%), migraine. (15.8%) and rheumatoid arthritis . (9.2%) In STEMI; Stress life style. (33.3%), both of (Migraine & HCV). (28.3%) and myocardial bridge (19%). In Non-STEMI; Stress life style. (28.3%), S.L.E. (24.5%) and migraine (11.3%). The main three gynaecological risk factors effect on ACS subtypes: In unstable angina : Preeclampsia and/or eclampsia (P/E) 30.3%, oral contraceptive pills. (O.C.P.) 19.7% and invitro fertilization hormonal treatment (I.V.F.ttt) 17.1%. In STEMI: Intramuscular injection contraceptive (I.M.I.c.) 33.3%, Preeclampsia and/or eclampsia (P/E)

32.8% and Chemotherapy 14.3%. In Non- STEMI: Intramuscular injection contraceptive (I.M.I.c.) 26.4%, Preeclampsia and/or eclampsia (P/E) 20.8% and gestational diabetes (Ges D) 15.1%. **Table 4**

Table 4: Nontraditional and gynecological risk factors of acute coronary syndrome.

	U.A No. %	**STEMI** No. %	**Non-STEMI** No. %
Non-Traditional Risk Factors			
S.L. S	54 (35.5 %)	14 (33.3 %)	30 (28.3 %)
Rh.A	14 (9.2 %)	2 (4.8 %)	8 (7.5 %)
S.L. E	4 (2.6 %)	4 (9.5 %)	26 (24.5 %)
Migraine	24 (15.8 %)	10 (23.8 %)	12 (11.3 %)
MB.	6 (3.9 %)	8 (19.0 %)	4 (3.8 %)
CU. S	6 (3.9 %)		4 (3.8 %)
HCV.	12 (7.9 %)	10 (23.8 %)	10 (9.4 %)
Gynecological Risk Factors			
P / E	46 (30.3 %)	10 (23.8 %)	22 (20.8 %)
Ges.D	14 (9.2 %)	4 (9.5 %)	16 (15.1 %)
PCOS	8 (5.3 %)	4 (9.5 %)	8 (7.5 %)
H / O	8 (5.3 %)	4 (9.5 %)	10 (9.4 %)
I.V.F.ttt	26 (17.1 %)	2 (4.8 %)	6 (5.7 %)
Chemo.	14 (9.2 %)	6 (14.3 %)	6 (5.7 %)
Radio.	8 (5.3 %)	4 (9.5 %)	6 (5.7 %)

I.M.I.c	24 (15.8 %)	14 (33.3 %)	28 (26.4 %)
O.C. P	30 (19.7 %)	4 (9.5 %)	14 (13.2 %)

Data are presented as frequency (%). U. A: Unstable angina, STEMI: ST elevated myocardial infarction, Non-STEMI: Non-ST elevated myocardial infarction, S.L.S.: stress lifestyle, Rh.A: rheumatoid arthritis, S.L.S.: systemic lupus erythematosus, MB: myocardial bridge, CU.S: Cushing syndrome, HCV: hepatitis C virus. P/E: preeclampsia +/- eclampsia, Ges.D: gestational diabetes, PCOS: polycystic ovary syndrome, H/O: hystrectomy +/- oophorectomy, I.V.F. ttt.: invetro fertilization hormonal treatment, Chemo.: chemotherapy for breast cancer, Radio.: radiotherapy for breast cancer, I.M.I.c: intramuscular injection contraceptive, O.C.P.: oral contraceptive pills.

Distribution of acute coronary syndrome risk factors among the studied patients. **Table 5**

Table 5: Distribution of acute coronary syndrome risk factors among the studied patients and number of patients related to number of risk factors in each group

Risk factor group	**Traditional risk factors No. (%)**	**Nontraditional risk factors No. (%)**	**Gynecological risk factors No. (%)**
No. of Patients	298 (99.3 %)	184 (61.3 %)	242 (80.7 %)
Number of patients related to number of risk factors in each group			
No Risk Factor	2(0.7 %)	116 (38.7 %)	58(19.3 %)
1 Risk Factor	28 (9.3 %)	122 (40.7 %)	152(50.7 %)
2 Risk Factors	72 (24.0 %)	46 (15.3 %)	76 (25.3 %)
3 Risk Factors	124 (41.3 %)	14 (4.7 %)	12 (4.0 %)
4 Risk Factors	62 (20.7 %)	2 (0.7 %)	2 (0.7 %)
5 Risk Factors	12 (4.0 %)		

Data are presented as frequency (%).

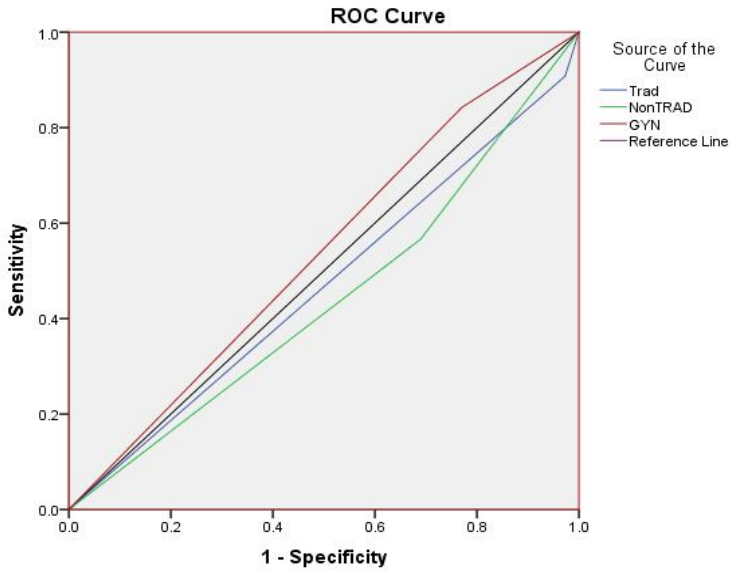
Distribution of risk factors in acute coronary syndrome subtypes and representation of number of risk factors for each patient in the current study. **Table 6**

Table 6: Percentage distribution of risk factors in acute coronary syndrome subtypes and representation of number of risk factors for each patient in the current study

	1 R.F	**2 R. F**	**3 R. F**	**4 R. F**	**5 R. F**	**6 R. F**	**7 R. F**	**8 R. F**	**9 R. F**	**10 R. F**
U.A.	0.0 %	5.3 %	11.8%	27.6%	33.0%	7.9 %	9.2 %	3.9 %	0.0 %	1.3 %
STEMI	0.0 %	4.8 %	0.0 %	14.3%	19.0%	47.6%	4.8 %	9.5 %	0.0%	0.0 %
Non -STEMI	0.0 %	3.8 %	15.1%	28.3%	20.8%	16.9%	15.1%	0.0 %	0.0 %	0.0 %
Risk factor for each patient:										
Patients	0	14	34	78	80	50	32	10	0	2
Representation in the sample	0 %	4.7 %	11.3 %	26 %	26.6 %	16.7 %	10.7 %	3.3 %	0 %	0.7 %

U. A: Unstable angina, STEMI: ST elevated myocardial infarction, Non-STEMI: Non-ST elevated myocardial infarction, R.F: risk factor/s

The sensitivity of ROC curve to the 1st group (Traditional risk factors) was 90.8% and for the 3rd group (Gynecological risk factors) was 84.2% while the sensitivity of ROC curve to the 2nd risk factor group (Nontraditional risk factors) was only 56.6%. The specificity of ROC curve to the 1st group was 97.3% and in the 3rd group was 77% while it decreased in the 2nd group to be 68.9%. **Figure 2**



ROC: Receiver operating characteristic curve

Figure 2: ROC curve analysis of risk factors groups of acute coronary syndrome

Relationship between ACS risk factors and severity of coronary artery stenosis which assessed by SYNTAX score:

There was positive correlation between age and SYNTAX score (R = 0.192) and a statistical significance between the age and the SYNTAX score was detected (P = 0.012). There was positive correlation between traditional risk factors and syntax score. (R = 0.259) and there was also a statistical significance between this group and SYNTAX score. (P = 0.001). There was positive correlation between non-traditional risk factors and syntax score (R = 0.257) and a statistical significance between this group and the SYNTAX score was clear (P = 0.001). There was mild positive correlation between gynecological risk factors and syntax score (R = 0.073) while, there was no statistical significance between this group and the SYNTAX score. (P value was > 0.05). Finally, there was positive correlation and statistical significance between the total risk factors groups (A, B and C) and the SYNTAX score (R = 0.395, P = 0.001). **Table 7**

Table 7: Correlation between SYNTAX score and each group of ACS risk factors and between total ACS risk factors and SYNTAX score

Acute Coronary Syndrome subgroups	Syntax Score		Significance
	R	**P- value**	
Age	0.192	0.012 *	**S**
Traditional risk factors	0.259	0.001 *	**S**
Non-traditional risk factors	0.257	0.001 *	**S**
Gynecological risk factors	0.073	0.341	**NS**
Total risk factors	0.395	0.001*	**S**
SYNTAX score	Unstable angina	STEMI	Non-STEMI
Range	16 -20	23 - 29	18 - 26
Mean ± SD	18.04 ± 1.07	25.74 ± 1.27	22.09 ± 1.50
F. test	250.597		
P. value	0.001 *		

*: Significant P value

From the ANOVA analysis, Sig. = 0.001 (less than 0.05), so the regression analysis is significant and there is a relationship between the independent variable (ACS risk factors- group A and group B) and the dependent variable (SYNTAX score) while in group c Sig. = 0.18 (greater than 0.05), so the regression analysis is insignificant and there is no clear relationship between the independent variable (ACS risk factors- group C) and the dependent variable (SYNTAX score), and Sig.F = 0.0001, so the regression analysis is significant and there is a relationship between the independent variables (ACS risk factors- groups A, B, C. together) and the dependent variable (SYNTAX score).**Table 8**

Table 8: ANOVA (ACS- group A: traditional risk factors, Group B: Non-traditional risk factors, Group C: Gynecological risk factors)

		df	*SS*	*MS*	*F*	*Significance F*
Group A	**Regression**	1	71.766	71.766	9.957	0.002*
	Residual	168	1210.822	7.207		
	Total	169	1282.588			
Group B	**Regression**	1	66.718	66.718	9.218663476	0.002*
	Residual	168	1215.869	7.237		
	Total	169	1282.588			
Group C	**Regression**	1	13.533	13.532	1.791	0.1825
	Residual	168	1269.055	7.553		
	Total	169	1282.588			
Group A, B, C	**Regression**	3	148.773	49.59	7.260525	0.0001
	Residual	166	1133.815	6.83		
	Total	169	1282.588			

df: Degree of freedom, **SS**: Sum of squares for between group variability, **Ms**: mean square, *: significant

P value: less than 0.005, there is indicating the significance of coefficient of the independent variables i.e., the Group A, group B, group C and groups A, B, C on the level of SYNTAX score in ACS. **Table 9**

Table 9: Coefficient table (ACS group A, B, C and ABC)

Group A	*Coefficients*	*Standard Error*	*t Stat*	*P-value*
Intercept	20.405	0.615	33.160	1.24069E-75
A	0.622	0.197	3.155	0.001*
Group B				
Intercept	21.542	0.307	69.99	3.3478E-126

B	0.756	0.248	3.036	0.002*
Group C				
Intercept	21.861	0.350	62.415	3.7559E-118
C	0.331	0.247	1.338	0.182
Groups A, B, C				
Intercept	19.386	0.692	27.983	9.66082E-65
A	0.547	0.194	2.816	0.005*
B	0.741	0.248	2.977	0.003*
C	0.494	0.239	2.064	0.040*

*: significant P value

Stepwise multi regression analysis

Stepwise multiple regression analysis of traditional, non-rational and gynaecological risk factors for predication of SYNTAX score, in the current study

In the current study, hypertension, diabetes mellitus, chronic kidney disease, obesity, systemic lupus erythematosus, myocardial bridge, cushion syndrome and radiotherapy for breast cancer were significantly independently correlated to the SYNTAX score. The hypertensive patient was exposed to acute coronary syndrome more likely than non-hypertensive woman by 2.6 folds. (P-value = 0.001). The diabetic patient was exposed to acute coronary syndrome more likely than the non-diabetic patient by 1.2 folds. (P-value = 0.018) *The chronic kidney disease patient was exposed to acute coronary syndrome more likely than non-kidney diseased patient by 1.1 folds. (P-value = 0.030). The obese patient was exposed to acute coronary syndrome more likely than non-obese patient by 0.7-fold. (P-value = 0.039). The systemic lupus erythematosus patient was exposed to acute coronary syndrome more likely than non-systemic lupus erythematosus patient by 1.2 folds. (P-value = 0.021). The myocardial bridge patient was exposed to acute coronary syndrome more likely than non-myocardial bridge patient by 11.3 times. (P-value = 0.001). The cushion syndrome

patient was exposed to acute coronary syndrome more likely than non- cushion syndrome patient by 0.5-fold. (P-value = 0.046). The radiotherapy for breast cancer was exposed to acute coronary syndrome more likely than other patients who not received radiotherapy by 0.68-fold (P-value = 0.015). Table 10

Table 10: Stepwise multi regression analysis

Risk factors of acute coronary syndrome	OR (95% CI)	P value
Dyslipidemia	0.786 (0.786 – 4.254)	0.161
HTN	2.613 (2.613 – 27.034)	0.001*
DM	1.230 (1.230 – 8.646)	0.018*
CKD	1.140 (1.140 – 13.623)	0.030*
Thyroid dysfunction	0.216 (0.216 – 5.664)	0.903
Sm.	0.163 (0.163 – 10.425)	0.802
Obesity	0.743 (0.743 – 8.392)	0.039*
S.L. S	0.447 (0.447 – 3.312)	0.701
Rh. A	0.553 (0.553 – 12.878)	0.221
S.L. E	1.218 (1.218 – 10.848)	0.021*
Migraine	0.642 (0.642 – 10.125)	0.184
M.B.	11.305 (11.305 – 921.153)	0.001*
HCV.	0.210 (0.210 – 23.351)	0.508
CU. S	0.494 (0.494 – 0.576)	0.046*

P/E	0.289 (0.289 – 2.115)	0.628
Ges. D	0.796 (0.796 – 9.860)	0.109
PCOS	0.201 (0.201 – 6.785)	0.862
H/O	0.339 (0.339 – 11.693)	0.446
I.V.F. ttt	0.084 (0.084 – 5.031)	0.679
Chemo.	0.313 (0.313 – 10.925)	0.498
Radio.	0.683 (0.683 – 57.991)	0.015*
Contraception	0.497 (0.497 – 3.861)	0.533

*: significant, HTN: hypertension, DM: diabetes mellitus, CKD: chronic kidney disease, thyroid dysfunction, Sm: Smoking, S.L.S: Stress life style, Rh.A.: Rheumatoid arthritis, S.L.E.: Systemic lupus erythematosus, M.B.: Myocardial bridge, HCV: Hepatitis C virus, Cu.S: Cushion syndrome, P/E: Preeclampsia / or eclampsia, Ges.D: Gestational diabetes, PCOS: Polycystic ovary syndrome, H/O: Hysterectomy and / or oophorectomy, I.V.F.ttt: In vetro fertilization hormonal treatment, Radio: radiotherapy, O.C.P.: oral contraceptive pills, .M.Ic: intramuscular injection contraceptives

Availability of data and materials

The data used to support the findings of this study are included within the article.

Discussion:

The mortality rate of ACS in young women after discharge is higher than in men. This is mainly due to poor medical follow up or the heavy burdens of living. ACS due to acute plaque rupture is associated with established risk factors including hypertension, diabetes mellitus, dyslipidemia and smoking [6].

In the present study, it was noted that obesity formed about 84.7% of the study sample (grade 1 obesity in which BMI = 30 to 34.9) formed 47.4% of total unstable angina cases and grade

1 obesity also formed 37.7% of the total non-STEMI cases, while grade 2 obesity, in which BMI = 35 to 39.9, formed 47.6% of total STEMI cases.

Also, in this study, total dyslipidemia (including patients who suffered from hypercholesterolemia, hypertriglyceridemia, or both (who showed an increase in serum cholesterol and triglycerides together) was reported in 48.6%. However, LAD was also the main affected artery among the subjects in the current study. This controversy could be explained by the genetic differences.

This is in agreement with previous study by Davidson, Laura, et al. [7], they noted that ACS in a sample of 124 young patients was caused by traditional risk factors (obesity, hyperlipidemia and smoking) and noted that 49% of the patients were obese (with a body mass index more than 30).

The present study disagreed with study by Beckowski Maciej, et al. [8], which was noted that the major risk factor which predisposed acute coronary syndrome in 1941 young women aged below 45 years was hypertension (49.8%). The second common risk factor was smoking, accounting for 48.7%, while hypercholesterolemia formed about 36.1% and obesity was 22.3%. Lastly, they found that diabetes mellitus formed 10.6% of total risk factors.

As in our study obesity was the main risk factor of ACS in young females (84.7%), then comes hypertension (61.3%) and stressful lifestyles (32.7%), while dyslipidemia (hypercholesterolemia) formed only 25.3% of total risk factors. The percentage of patients with diabetes mellitus was totally 40%, while type 2DM was more than type 1. That was due to unhealthy eating habits in Egypt, irregular eating times and delayed dinner times, leading to a remarkable increase in overweight, obesity and diabetes mellitus (specially type 2).

In a retrospective study by Norsa' adah B, et al. [9], the sample of their study included 147 ACS patients aged below 45years. The study found that dyslipidemia was the main risk factor

of ACS (65.3%), hypertension came second with 43.5%, while obesity formed 27.2% and diabetes mellitus 25.9%.

In the current study, however, obesity formed about 84.7% of total obesity classes, while total dyslipidemia subtypes formed 48.6% and diabetes mellitus (type 1 and type 2) about 40% of our cases.

In another study by Parizad Razieh et al. [10] on 101 women of reproductive age period stage (between 15 to 45 years) who were admitted to hospital with ACS with a mean age of 39.5 years. Unstable angina (UA) was reported in 49%, STEMI cases was reported in 30%, and the percentage of non-ST elevated myocardial infarction (non-SEMI) was 29%.

The current study was disagreed in the following points: *The mean age was 41.18 years. Unstable angina was noted in 50.7%, ST elevation myocardial infarction was formed in 14%, while the percentage of non-STEMI was 35.3%.

*Also in that study, about 42% of total cases were exposed to percutaneous coronary intervention and stent implantation (PCI) or coronary artery bypass graft surgery (CABG), while in the current study, about (56%) of cases were exposed to PCI.

In the current study, though, the main traditional risk factors were Obesity which formed 84.7%, hypertension in the second stage with 61.3%, total diabetes mellitus (40%), while stressful lifestyles formed 32.7%. The total dyslipidemia percentage in our study formed 48.6%, and oral contraceptive pills was the third main cause (16% of the cases), while the first gynecological risk factor was pre-eclampsia and/or eclampsia (P/E) by a percentage of 26% followed by the intramuscular injection of contraceptive method (IMIc) (22%).

In that study, the medical therapy of ACS cases was present in 52.7% (distributed as follows: UA=26.4%, STEMI= 15%, non-STEMI= 11.3). The exposure to PCI as a line of management was found in 30.1% of ACS cases (distributed as follows: UA= 13.2%, STEMI= 9.4%, non-STEMI= 7.5%). While in the current study, the medical therapy of ACS

cases was present in 43.3% (distributed as follows: UA= 81.6%, STEMI= 9.5%, non-STEMI= 1.9%). Using PCI as a line of management was found in 56.6% of total cases in our study (distributed as follows: UA= 18.4%, STEMI= 90%, non-STEMI= 98%).

In the present study, there were some disagreements with that study in the form of: Unstable angina (UA) was considered as the major ACS subtype (50.7%), followed by non-ST segment elevation myocardial infarction (non-STEMI) was (35.3%) and finally the ST segment elevation myocardial infarction (STEMI) which was noted in 14% of the total ACS cases. In another single center prospective observational study in India by Mahajan, et al. [11] they classified the study sample into two groups (Group 1: female patients aged less than 45 and group 2: aged from 45 to 55 years). They noted that obesity or overweight (BMI equal to or more than 23 k/m2) formed 49.5% in the first group and formed 56.8% in the second.

There was disagreement in the present study: and according to the World Health Organization-BMI, obesity classification (Feb.2014), overweight started from BMI 25 kg/m2 and obesity started from 30 kg/m2. The current study found that: the percentage of overweight was 14.7% and obesity formed 84.7%.

Also, in Mahajan et al., [11] they found that hypertension was found in 55.6% of patients less than 45 years and in 64.5% of patients of the age group from 45 to 55 years, while diabetes mellitus was found in 10.1% and 26.8% respectively in these two age subgroups.

In the present study, most patients admitted with unstable angina refused coronary intervention and only 28 cases accepted coronary artery intervention and PCI, showing a different distribution of coronary lesion sites (RCA lesions in 7.9%, LAD lesions in 6.6% and finally LCX lesions in 3.9% of the total PCI in unstable angina cases. Compare the recent two types of ACS (STEMI and Non-STEMI), it was noted the following coronary arteries lesion sites distribution: LAD was 66.7% in STEMI and 64.2% in Non-STEMI., RCA was 47.6% in STEMI and 37.7% in Non-STEMI., LCX was 42.9% in STEMI and 34% in Non-STEMI.

In a retrospective study by Venkatason Padmaa, et al. [12] which discussed the characteristics and short-term outcomes of young women diagnosed with acute myocardial infarction in Malaysia throughout the period from 2006 to 2013. They divided female patients into two groups according to age: the first included 292 cases of young females aged below 45 years and the second included old females aged more than 45 years. This retrospective study identified the main risk factors of acute myocardial infarction in the first group and included the following: Hypertension (57.7%), then Diabetes mellitus (55.7%), Dyslipidemia (37.8%), Smoking (9.6%) and Chronic renal failure (5.3%). This study compared between the percentages of myocardial infarction subtypes among these patients and found out that STEMI- ACS formed 29.3% while Non-STEMI-ACS formed 18.1%.

In a recent study by: El Kersh, A., Reda, A., El Hadad, M. *et al.;* [13] they investigated the relationship between conventional risk factors of CAD with its complexity using SYNTAX score. In 52 ischemic heart disease patients who admitted to elective coronary angiography. The overall SYNTAX score was calculated prospectively for each case. Then a comparison study was done between populations with and without each risk factor. There was a statistically significant correlation between age, hypertension, diabetes mellitus, dyslipidemia and smoking with SYNTAX score results ($p < 0.05$) and an insignificant correlation regarding body mass index and gender ($p > 0.05$). it revealed that aging, having diabetes mellitus and smoking were identified as significant independent risk factors for CAD complexity. The conclusion of that study said that: Advanced age, having diabetes mellitus and cigarette smoking are considered to be independent risk factors for the complexity of CAD. Therefore, when these factors present, the expectation of the SYNTAX score of the ischemic heart disease patient be high which indicate a complex CAD.

The present study There was a positive relationship between the increase total number of ACS risk factors subgroups (Either traditional, nontraditional, or gynecological risk factors) and the degree of coronary artery stenosis that assessed by SYNTAX scorer

Study limitations

The recurrent wave of COVID-19 pandemic had a negative impact on the rate of admission. Cardiac family history of most admitted patients was not clear for many patients. Many female patients refuse any forms of coronary artery intervention. Some patients refuse to do even a diagnostic CT scan of the coronary. Some patients neglect post discharge follow-up at the out clinic

Conclusions:

There was a clear positive relationship between the presence of many numbers of ACS risk factors in Egyptian women during their reproductive age period and the rate of occurrence of ACS. By the presence of several factors of ACS risk factors groups (traditional, nontraditional, gynecological) together in the affected female patients who suffered from any ACS subtype (unstable angina, STEMI or Non- STEMI) a significant effect occurred either on the severity or the degree of stenosis of the affected coronaries, more than the effect of each ACS risk factors subgroup separately on the affected coronary artery.

There was a moderate positive relationship between the increase total number of ACS risk factors subgroups (Either traditional, nontraditional, or gynecological risk factors) and the severity and degree of coronary artery stenosis that assessed by SYNTAX scorer. (The more risk factors in each group, the high-level SYNTAX score was noted) mainly in the traditional and nontraditional ACS subgroups (P-value < 0.05). While it was nonsignificant in the gynaecological risk factors subgroup separately (P-value > 0.05).

List of abbreviations

ACS: Acute coronary syndrome

ASCVD: Atherosclerotic cardiovascular disease risk score

WISE: Women′s Ischemic Syndrome Evaluation

UA: Unstable angina

STEMI: ST elevated myocardial infarction

Non-STEMI: Non-ST elevated myocardial infarction

CABG: Coronary artery bypass graft surgery

CK-MB: Creatine Kinase MB

BMI: Body mass index

PCI: Percutaneous coronary stent implantation

LM: Left main coronary artery

LAD: Left anterior descending coronary artery

RCA: Right coronary artery

LCX: Left circumflex coronary artery

TG. & Chol.: Hypertriglyceridemia and hypercholesterolemia

DM: Diabetes mellitus

CKD: Chronic kidney disease

P/E: Preeclampsia and/or eclampsia

I.M.I.c: Intramuscular injection contraceptive

Ges D: Gestational diabetes

S.L.S.: Stress lifestyle

Rh.A: Rheumatoid arthritis

S.L.S.: Systemic lupus erythematosus

MB: Myocardial bridge

CU. S: Cushing syndrome

HCV: Hepatitis C virus

PCOS: Polycystic ovary syndrome

H/O: Hystrectomy +/- oophorectomy**,**

I.V.F. ttt.: Invetro fertilization hormonal treatment

Chemo.: Chemotherapy for breast cancer

Radio.: Radiotherapy for breast cancer

O.C.P.: Oral contraceptive pills

ROC: Receiver operating characteristic curve

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