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Original Article

Serum Homocysteine level in the setting of acute coronary syndrome in young adult patients

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Abstract

Background: Acute coronary syndrome is a major cause of illness and death worldwide. Homocysteine serves as a noteworthy biomarker for assessing the overall state of an individual's health. **Aim:** The purpose of the study was to compare the level of homocysteine in young and elderly acute coronary syndrome patients, and investigate the correlation between homocysteine levels and other risk factors of acute coronary syndrome. **Methods:** The current study was cross-sectional. It was conducted at Internal Medicine Department and Coronary Care Unit of Sohag University Hospitals during the period from January 2022 to May 2023. The study involved one hundred patients diagnosed with acute coronary syndrome. They were classified into two groups according to age. Group (A) comprised 50 patients aged between 18- 40 years, and group (B) involved 50 patients aged 40 years and more. A complete history, clinical assessment, laboratory testing (cardiac enzymes, lipid profile and homocysteine level), ECG, and echocardiogram were carried out on every patient. **Results:** Most cases in group A and B had high homocysteine levels. There was no significant statistical difference between both groups. The homocysteine level in group A showed a positive correlation with triglycerides and a negative correlation with HDL. There was a negative correlation in group B between systolic, diastolic blood pressure and homocysteine levels. **Conclusion:** Homocysteine level was elevated in most cases of acute coronary syndrome; so it is crucial to investigate its level as a significant risk factor of acute coronary syndrome.

Keywords: Acute coronary syndrome, Homocysteine, Atherosclerosis

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Introduction

Acute coronary syndrome (ACS) is a major global killer.[1-2] Although ACS is more common in the elderly, its prevalence in young adults has been rising in the last years.[3-4]Many traditional risk factors like smoking, obesity, and hyperlipidemia have been associated with ACS in younger ages. New markers like hyperhomocysteinemia have emerged in relation with ACS. Moreover, high homocysteine levels are closely related to severity of ACS. [5]

Homocysteine (Hcy), an amino acid that contains sulfur, is created when methionine is converted to cysteine. [6] There is a direct association between Hcy elevated levels and numerous clinical

conditions, as bone health, [7.8] neurodegenerative disease, [9] renal dysfunction, [10] cognitive impairments, [11] and the development of congenital defects. [12]

Furthermore, elevated homocysteine level is a risk factor for cerebrovascular disorders. [13-15] Patients, with cardiovascular disease who have high Hcy, have a significantly higher risk of development of atherosclerotic vascular disease and hypercoagulability conditions. [16-17]

The current study aimed to compare the level of homocysteine in young and elderly acute coronary syndrome patients, and study the correlation between homocysteine level and other risk factors of acute coronary syndrome.

Patients and methods

The current study was a cross-sectional. It was carried out from January 2022 to May 2023 at Internal Medicine Department and Coronary Care Unit of Sohag University Hospitals.

One hundred patients with acute coronary syndrome were included in the study. Patients were classified into two groups; group (A) included 50 patients aged between 18- 40 years and group (B) involved 50 patients aged 40 and more.

Inclusion criteria:

Patients aged 18 years old or more presented with chest pain consistent with ACS by ECG changes, and high troponin T level (Normal value < 0.06 ng/mL).

Exclusion criteria:

Patients with rheumatic heart disease, congenital heart disease, chronic kidney disease, anemia and cancer were excluded.

The participants were subjected to history taking, clinical assessment, laboratory testing (cardiac enzymes, lipid profile and homocysteine level), ECG and echocardiography.

According to the results of both ECG and cardiac troponin T level, ACS was classified into unstable angina (UA), ST-segment elevation myocardial infarction (STEMI), Non ST-segment elevation myocardial infarction (NSTEMI). [18]

Ethical considerations:

The Medical Research Ethics Committee at Sohag University's Faculty of Medicine authorized the research procedure. Clinical Trial.gov Identifier: NCT05125419. Written informed consent was provided by each patient to participate.

Statistical analysis:

Data were collected and analyzed using IBM's Statistical Package for the Social Sciences (SPSS) (version 26.0. Armonk, NY: IBM Corp). To ensure a normally distributed sample, we employed the Kolmogorov-Smirnov test. Mean ± SD, and median were used for quantitative data, while numbers and percentages were used for qualitative data. Chi-square, Fischer Exact, Student T, and Mann Whitney tests were utilized. Spearman's technique was used to analyze the correlation. Significant difference was considered at p-value < 0.05.

Results

The participants were 100 patients with chest pain consistent with ACS. According to age, they were separated into two groups. Group (A) included 50 patients aged between 18- 40 years and group (B) involved fifty patients aged ≥ 40 years old. Group (A) had an average age of 36.06± 3.88 years, while group (B) had an average age of 56.84± 9.49 years. In group (A), there were 40 (80%) males and 10 (20%) females, whereas in group (B), there were 42 (84%) males and 8 (16%) females (Fig.1).

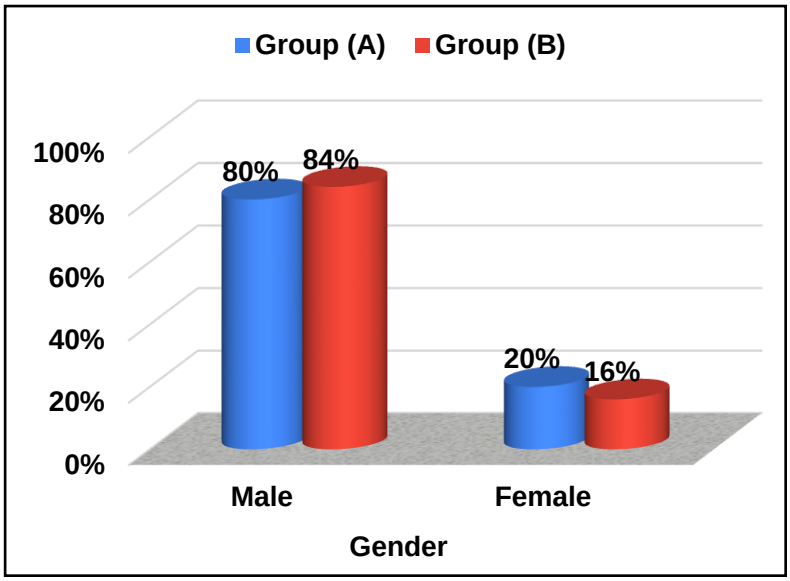

Figure (1): Comparison between study groups regarding gender.

Regarding risk factors and medical history in group (A), 11 (22%) patients were diabetics, 7 (14%) patients were hypertensive, 8 (16%) had family history of coronary artery disease (CAD), 24 (48%) were current smokers, and 2 (4%) had previous history of percutaneous coronary intervention (PCI). In group (B), 14 (28%) patients were diabetics, 17 (34%) patients were hypertensive, 3 (6%) had family history of CAD, 26 (52%) were current smokers, 6 (12%) had previous history of PCI, one (2%) had previous history of coronary artery bypass grafting (CABG) and one (2%) had prior stroke. The percentage of patients with hypertension was significantly higher in group B than in group A (p = 0.019). However, there was no statistically significant difference (p > 0.05) between the two groups for the other risk factors (Table 1).

Table (1): Comparing the studied groups regarding risk factors and medical history

Risk factors and medical history	Group (A) 18- 40 years (No. = 50)		Group (B) ≥ 40 years (No. = 50)		Chi-Square test P-value
Diabetes mellitus	11	22%	14	28%	0.488
Hypertension	7	14%	17	34%	**0.019***
Smoking	26	52%	34	68%	0.071
Family history of CAD	8	16%	3	6%	0.11
Prior PCI	3	6%	6	12%	0.487 FET
Prior CABG	0	0%	1	2%	1.00 FET
Prior Stroke	0	0%	1	2%	1.00 FET

** Significant difference at p-value < 0.05. FET: Fischer Exact test. CAD: coronary artery disease. PCI: percutaneous coronary intervention. CABG: Coronary arteries bypass grafting.*

Regarding the therapeutic history, there was a statistically significant difference (p = 0.044) between the two groups. Group A exhibited significantly more insulin therapy, whereas group B showed significantly greater statin and ACE inhibitor therapy (table 2).

Table (2): Comparison between the studied groups concerning therapeutic history

		Group (A) 18- 40 years (No. = 50)		Group (B) ≥ 40 years (No. = 50)		Chi-Square Test	
		No.	%	No.	%	X^2	P-value
Therapeutic history	No	32	64%	21	42%	15.9	0.044*
	Aspirin	3	6%	5	10%		
	CCBs	0	0%	8	16%		
	B-blocker	6	12 %	8	16%		
	ACE inhibitor	5	10%	9	18%		
	ARBs	3	6%	5	10%		
	Clopidogrel	3	6%	7	14%		
	Statin	6	12%	11	22%		
	Oral hypoglycemic drugs	1	2%	8	16%		
	Insulin	10	20%	6	12%		

** Significant difference at p-value < 0.05. X^2: Chi-Square Test. CCBs: calcium channel blockers. ACE: angiotensin-converting enzyme. ARBs: angiotensin receptor blockers.*

Regarding diagnosis, 28% of patients had NSTEMI, 64% of them had STEMI and 8% diagnosed as unstable angina in group A. However in group B, 26% of patients had NSTEMI, 62% of them had STEMI and 12% of them had unstable angina. The two groups showed no significant statistical difference (Fig.2).

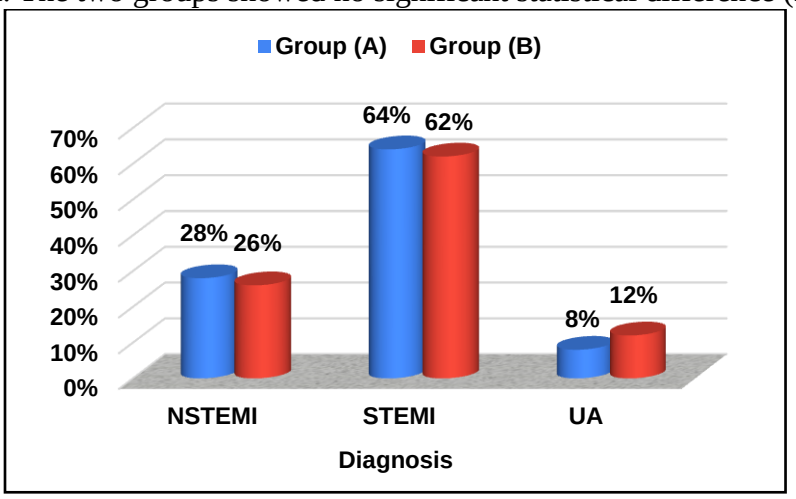

Figure (2): Comparison of the study groups regarding diagnosis.

NSTEMI: Non ST-segment elevation myocardial infarction. STEMI: ST-segment elevation myocardial infarction. UA: unstable angina.

In group A, the mean systolic and diastolic blood pressure were 121.25 ± 14.53 and 78.54 ± 10.31 mm/Hg respectively. The mean heart rate was 86.16 ± 12.83 beats/ min. In group B, the mean systolic and diastolic blood pressure were 122.2 ± 20.53 mm/Hg and 78.2 ± 13.2 mm/Hg respectively. The mean heart rate was 90.26 ± 20.63 beats/ min. There were no significant statistical differences between the two studied groups ($p > 0.05$) (table 3).

Table (3): Comparison of the vital signs in the studied groups

	Group (A) 18- 40 years (No. = 50)					Group (B) ≥ 40 years (No. = 50)					Mann-Whitney U Test	
	Mean	± SD	Median	Min.	Max.	Mean	± SD	Median	Min.	Max.	Test value	P-value
Systolic BP (mm/Hg)	121.25	14.53	120.0	90.0	160.0	122.2	20.53	120.0	90.0	170.0	0.036	0.971
Diastolic BP (mm/Hg)	78.54	10.31	80.0	60.0	100.0	78.20	13.2	80.0	60.0	100.0	0.210	0.834
Heart rate (beats/min)	86.16	12.83	87.0	62.0	110.0	90.26	20.63	90.0	50.0	160.0	0.726	0.468

Significant difference at p-value < 0.05. SD: standard deviation. BP: blood pressure

There was no statistically significant difference (p > 0.05) in clinical examination between the two groups under study (table 4).

Table (4): Comparing the studied groups regarding clinical examination

		Group (A) 18- 40 years (No. = 50)		Group (B) ≥ 40 years (No. = 50)		Chi- Square test	
		No.	%	No.	%	X^2	P-value
Chest examination	**Clear**	46	92%	44	88%	0.521	0.771
	Fine basal crepitation	3	6%	4	8%		
	Scattered crepitation all over the chest	1	2%	2	4%		
Abdominal examination	**Clear**	50	100%	50	100%	-	-
Cardiac examination	**Clear**	50	100%	50	100%	-	-
Lower limb edema	**No**	47	94%	48	96%	0.211	1.00^{FET}
	Yes	3	6%	2	4%		

Significant difference at p-value < 0.05. X^2: Chi-Square Test. FET: Fischer Exact test.

Troponin and Creatine Kinase MB (CK-MB) levels were positive in 92% of the patients in group A. However, in group B 88% of patients had positive troponin and positive CK-MB. Between the two groups, there was no statistically significant difference (table 5).

Table 5: Comparing the cardiac markers between both groups

		Group (A) 18- 40 years (No. = 50)		Group (B) ≥ 40 years (No. = 50)		Chi- Square test	
		No.	%	No.	%	X^2	P-value
Troponin	**Negative**	4	8%	6	12%	0.444	0.505
	Positive	46	92%	44	88%		
CK-MB	**Negative**	4	8%	6	12%	0.444	0.505
	Positive	46	92%	44	88%		

Significant difference at p-value < 0.05. X^2: Chi-Square Test. CK-MB: Creatine Kinase MB

Considering serum triglycerides, total cholesterol, HDL, and LDL, there was no statistically significant difference between the two groups (p > 0.05) (table 6).

Table (6): Comparing the lipid profile in the studied groups

	Group (A) 18- 40 years (No. = 50)					Group (B) ≥ 40 years (No. = 50)					Mann-Whitney U Test	
	Mean	± SD	Median	Min.	Max.	Mean	± SD	Median	Min.	Max.	Test value	P-value
TG (mg/dl)	167.12	131.46	130.0	45.0	892.0	151.41	53.03	133.50	61.4	300.0	0.610	0.542
Cholesterol (mg/dl)	190.44	58.77	181.0	96.0	399.0	193.33	37.32	186.25	140.0	276.0	0.772	0.440
HDL (mg/dl)	42.80	13.53	39.50	23.0	79.0	45.43	11.32	44.90	27.0	79.0	1.393	0.164
LDL (mg/dl)	115.66	40.99	111.0	46.6	219.0	117.66	34.60	109.55	61.0	189.8	0.383	0.702

TG: triglycerides. HDL: high-density lipoprotein. LDL: low-density lipoprotein

The ECG and echocardiography results for the groups under study are displayed in Table 7. There was no statistically significant difference between them.

Table (7): Comparing the ECG and echocardiography findings in the two groups

		Group (A) 18- 40 years (No. = 50)		Group (B) ≥ 40 years (No. = 50)		Test value	P-value
		No.	%	No.	%		
ECG	**Biphasic T wave**	4	8.0%	1	2 %	X^2=5.78	0.328
	Inverted T wave	3	6.0%	5	10 %		
	LBBB	7	14 %	4	8 %		
	Pathological Q wave	1	2 %	3	6 %		
	ST segment depression	3	6 %	7	14 %		
	ST segment elevation	32	64 %	30	60 %		
SWMA	**No**	8	16 %	4	8 %	X^2= 2.346	0.309
	Hypokinesia	39	78 %	40	80 %		
	Akinesia	3	6 %	6	12 %		
EF (%)	**Mean ± SD**	48.29 ± 9.15		49.16 ± 10.49		T= 0.422	0.674
	Median	47		50			
	Range	32 - 66		23 - 72			

ECG: electrocardiogram. LBBB: left bundle branch block. SD: standard deviation. SWMA: Segmental Wall Motion Abnormality. EF: Ejection fraction. $X^{2:}$ Chi- Square test. T: Student T test

The majority of patients (66% in group A and 70% in group B) had high homocysteine level. The mean homocysteine levels in group A and B were 22.06 ± 9.84 µmol/ L and 22.96 ± 11.06 µmol/ L respectively. There was no statistically significant difference between both groups (table 8).

Table (8): Comparing the homocysteine level in the studied groups

		Group (A) 18- 40 years (No. = 50)		Group (B) ≥ 40 years (No. = 50)		Test value	P-value
		No.	%	No.	%		
Homocysteine level (µmol/L)	**Normal**	17	34%	15	30%	X^2= 0.184	0.668
	High	33	66%	35	70%		
	Mean ± SD	22.06 ± 9.84		22.96 ± 11.06		Z_{MWU} = 0.193	0.847
	Median	22.5		21.91			
	Range	7- 41		5 – 55.14			

Significant difference at p-value < 0.05. SD: standard deviation. X^2: Chi-Square Test. MWU: Mann-Whitney U Test.

In group (A) homocysteine level was positively correlated to triglycerides (r = 0.310, p = 0.028) and negatively correlated to HDL (r = -0.340, p = 0.016) (table 9, fig 3).

Table (9): Correlation between homocysteine level and different variables in group A

	Homocysteine level	
	r	p- value
Age (years)	-0.137	0.343
Systolic BP (mm/Hg)	-0.029	0.844
Diastolic BP (mm/Hg)	-0.014	0.926
Heart rate (beats/min)	-0.050	0.731
TG (mg/dl)	0.310	0.028*
Cholesterol (mg/dl)	0.180	0.210
HDL (mg/dl)	-0.340	0.016*
LDL (mg/dl)	0.210	0.144
EF (%)	-0.207	0.189

**Significant difference at p-value < 0.05. BP: blood pressure. TG: triglycerides. HDL: high-density lipoprotein. LDL: low-density lipoprotein. EF: Ejection fraction. r: Spearman Rho*

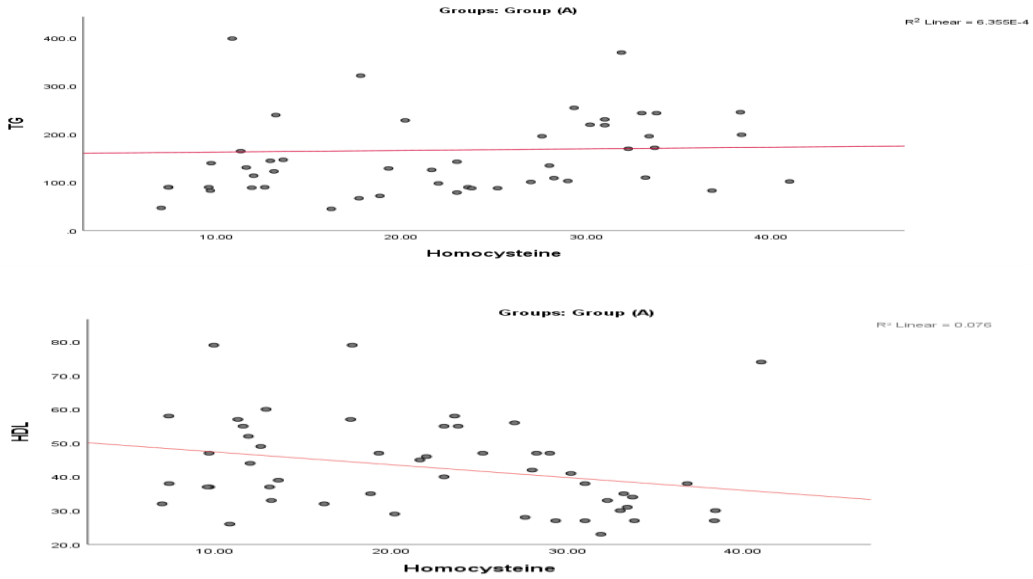

Figure 3- 3A: Scatter plot displaying positive correlation between homocysteine levels and triglycerides in group A. 3B: Scatter plot indicating negative correlation between homocysteine level with HDL in group A

In group B, homocysteine level is negatively correlated to systolic and diastolic blood pressure (r = -0.309, p = 0.029) (table 10, fig 4).

Table (10): Correlation between homocysteine level and different variables in group B

	Homocysteine level	
	R	**p- value**
Age (years)	-0.040	0.783
Systolic BP (mm/Hg)	-0.309	0.029*
Diastolic BP (mm/Hg)	-0.309	0.029*
Heart rate (beats/min)	-0.094	0.518
TG (mg/dl)	0.046	0.751
Cholesterol (mg/dl)	-0.103	0.477
HDL (mg/dl)	0.134	0.352
LDL (mg/dl)	-0.187	0.195
EF (%)	-0.146	0.317

**Significant difference at p-value < 0.05. BP: blood pressure. TG: triglycerides. HDL: high-density lipoprotein. LDL: low-density lipoprotein. EF: Ejection fraction. r: Spearman Rho*

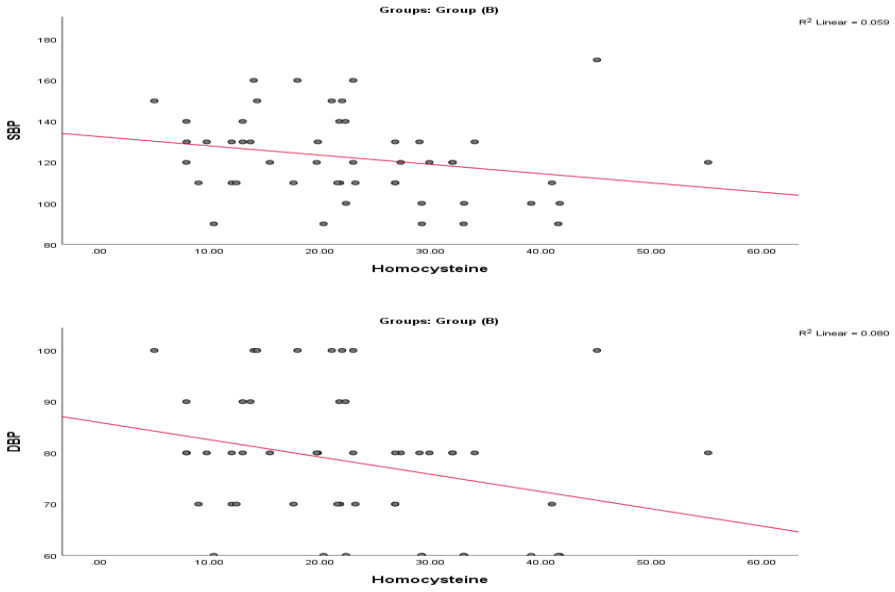

Figure 4- 4A: Scatter plot showing homocysteine level negatively correlated to systolic blood pressure in group B. 4B: Scatter plot showing homocysteine level negatively correlated to diastolic blood pressure in group B

Discussion

Cardiovascular illnesses are the leading cause of death around the world with 17.9 million deaths annually. (19) ACS contributes significantly to death from cardiovascular illnesses. (20)

A higher risk of atherosclerosis has been linked to high HCY levels. High HCY levels may also be associated with poor outcomes in patients with peripheral arterial disease, stable angina, and stroke. However, it is still unclear whether or not blood HCY levels are predictive in patients with (STEMI), which is caused by abrupt coronary occlusion. (21)

In the present study, group (A) consisted of 20% female cases and 80% male cases. While, group (B) consisted of 16% female cases and 84% male cases. There was no significant difference between both groups. This was in agreement with Al-Obaidi et al. (22) but disagreed with Miñana et al. (23) and Sun

et al. (24) This could be explained by the limited number of participants in the current study.

Regarding the risk factors, group B had a significantly greater number of hypertensive patients than group A (p = 0.019). Similarly, Calim et al. (25) found that the groups under study had significantly different levels of hypertension.

Other risk factors showed no significant difference among the two groups. This came in disagreement with Miñana et al. (23), who found that diabetes and smoking were also significant risk factors. The different results may be due to different population as they compared non STEMI patients with STEMI patients.

Regarding the therapeutic history, there was a statistically significant difference in the studied groups (p = 0.044). Group A had a much larger number of patients utilizing insulin therapy, whereas group B had a significantly greater proportion of patients taking statins and ACE inhibitors. This was consistent with the results of Calim et al. (25) who found that statin use differed significantly in the studied groups. However, Si et al. (20) discovered that there was no difference in the groups' treatment with ACE inhibitors and statins and a significant difference in calcium channel blocker.

Regarding diagnosis, 28% of patients had NSTEMI, 64% had STEMI and 8% were diagnosed as unstable angina in group A. However in group B, 26% of patients had NSTEMI, 62% of them had STEMI and 12% of them had unstable angina. The two groups did not significantly vary from one another (p > 0.05). This finding came in agreement with Miñana et al. (23)

Heart rate, blood pressure (systolic and diastolic), and lower limb edema did not significantly differ between the two groups in the current study (p > 0.05). This came in line with Si et al. (21)

In the current investigation, there was no statistically significant difference (p > 0.05) in blood triglycerides, total cholesterol, HDL, or LDL between the groups under investigation. Similar findings were reported by Si et al. (21) However, Sun et al. (24) reported a significant difference as regard lipid profile. The different result could be explained by the different populations.

In group A and B, the majority of cases had hypokinesia. The mean EF in group A and B were 48.29 ± 9.15 and 49.16 ± 10.49 respectively. Between the two groups, neither SWMA nor EF revealed a significant difference (p > 0.05). This agreed with Si et al. (21) Conversely, Miñana et al. (23) and Sun et al. (24) found that EF was significantly different between the studied groups.

Regarding homocysteine levels, there was no statistically significant difference (p > 0.05) between the majority of cases in groups A and B, despite their high levels. This came in disagreement with Begum et al. (26), who reported that the Hcy level in children and adolescents was greater than in adults. The difference in results could be explained by the smaller sample size they used (52 patients) and the different race (Asian) of the patients.

Homocysteine level in group A was positively correlated (r = 0.310, p = 0.028) and negatively correlated (r = -0.340, p = 0.016) to triglyceride and HDL levels respectively. The Hcy level in group B exhibited a negative correlation (r = -0.309, p = 0.029) with blood pressure (both diastolic and systolic). In contrast, Onyemelukwe et al. (27) observed that Hcy is positively correlated to blood pressure (systolic and diastolic). The disparity in ethnic group and population size may account for the various findings.

Conclusion

It was concluded that the majority of patients in groups A and B had elevated homocysteine levels. There was no significant difference in the homocysteine levels between young and elderly patients with acute coronary syndrome.

Among the young, the homocysteine level was positively correlated to triglycerides and negatively correlated to HDL. While in elderly, homocysteine levels were negatively correlated to blood pressure (systolic and diastolic).

Serum homocysteine elevation is an important risk factor for acute coronary syndrome that has to be investigated.

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