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Lipoprotein (A) Screening in Young and Middle Aged Patients Presented With Acute Vascular Ischemic Events (Myocardial Infarction & Cerebral Stroke)

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Abstract

Background: High lipoprotein (a) (LP (a)) is consider as an independent risk factor for Acute vascular ischemic events (e.g.: Myocardial infarction (MI) and ischemic stroke). However, Prior data from other large, population-based cohort studies have been conflicting on coronary artery disease and ischemic stroke, with some studies linking elevated Lp(a) levels to a higher incidence of myocardial infarction and ischemic stroke whereas others have not found any association.

Methods: Lp(a) had been measured for patients < 65 years of age presenting with myocardial infarction or ischemic stroke to cardiology and neurology departments in Mansoura University Hospitals, Dakahlia Governorate, Egypt, during the period from June 2020 to May 2022. Logistic regression model was used to determine the independent association of clinical characteristics with elevated Lp (a).

Results: A total of 103 patients were screened for Lp (a); 71.8 % males, mean age 50.7±7.9 years. Median Lp(a) levels were 26.3 mg/dl (interquartile range [IQR] 2-74). Elevated Lp(a) > 30 mg/dL was observed in 41.7% and associated with younger age with acute vascular ischemic events specially MI (48%). In a multiple logistic regression model, Family history of premature AVSE (MI & ischemic stroke) (odds ratio [OR] 3.36, 95% confidence interval [CI] 1.3-8.6, p = 0.01), younger age (< 45years) (p = 0.048) were independently associated with elevated Lp(a) in all cases of AVSE, in MI cases Family history of premature of CAD was more significant associated with high levels of Lp(a) (odds ratio [OR] 20.4, 95% confidence interval [CI] 2.3-174, p = 0.001), younger age (p=0.016) . In contrast, Lp(a) levels were not associated with other traditional cardiovascular risk factors in all cases of MI as a subgroup.

Conclusion: young and middle aged patients < 65y years presented with acute vascular ischemic event (MI and stroke) were independently associated with elevated Lp (a), especially in patients with MI, young aged and with FH for premature acute vascular ischemic event.

Keywords: Cardiovascular health; Patients; Acute

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Introduction

Lipoprotein (a) (Lp (a)) is a cardiovascular risk factor that has been under intense investigation in recent years [1]. Proposed mechanisms for its associated proatherosclerotic effects include a role in foam cell formation, promotion of cholesterol deposition into atherosclerotic plaques, and alterations in immunogenic responses [2, 3].

Lipoprotein (a) (Lp(a)) resembles to low-density lipoprotein (LDL) by the presence of one molecule Apo lipoprotein B (apoB) and its relatively high content of cholesteryl esters in the core. These features lend several in vitro atherogenic properties to Lp a) which are also exerted by LDL, for example proteoglycan binding and induction of foam cell formation [4].

Lp(a) differs from LDL by the presence of an additional Apo lipoprotein, termed apolipoprotein (a) (apo(a)), which is

covalently bound to apoB by one disulfide bond. Apo (a) is homologous to plasminogen by the presence of kringle IV and kringle V domains as well as a protease domain, which however is catalytically inactive. A variable number of repeat polymorphism of the kringle IV domain encodes for 40 apo (a) isoforms which differ by size and whose number is inversely correlated with Lp (a) plasma concentrations [5].

The similarity to plasminogen as well as the presence of oxidized phospholipids has been made responsible for the thrombogenic properties of Lp (a) which include the inhibition of fibrinolysis, the induction of plasminogen activator inhibitor type 1 (PAI-1) expression in endothelial cells, as well as the increasing of activity of tissue factor pathway inhibitor and platelet responsiveness [6]. Lp (a) levels are largely genetically determined and are thought to be only minimally affected by lifestyle [7]. This suggests that there may be an inherent predisposition to cardiovascular disease and stroke in people with elevated Lp(a). Given its aforementioned properties, proactive screening of patients with MI and stroke (especially those with premature events or a family history) will be needed, with particular attention placed on the screening of individuals with recurrent events despite adequate lipid lowering, who frequently have high Lp(a) [1, 8].

Prior data from other large, population-based cohort studies have been conflicting on coronary artery disease and stroke, with some studies linking elevated Lp (a) levels to a higher incidence of myocardial infarction and ischemic stroke, [9-12] whereas others have not found an association [13, 14]. This may be partly attributable to lack of differentiation between the subtypes of incident stroke or to racial or other differences in cohort composition. This may also be secondary to lack of adjustment for LDL-C levels, which is an important risk factor for stroke [1]. Also there is new study shows that increase in Lp (a) level more than 50mg/dL increases the risk of myocardial infarction in all populations except Arabs and Africans [15].

Patients and Methods

A-Technical Design

Setting: This study had been conducted in cardiology and neurology departments in Mansoura University Hospitals, Dakahlia Governorate, Egypt.

Population or Subjects: Patients who presented with acute myocardial infarction even STEMI or NSTEMI to cardiology department and patients presented with acute ischemic stroke (non-cardioembolic) to neurology department and their ages were less than or equal 65 y old.

Inclusion criteria / exclusion criteria

Inclusion criteria

For MI patients should fulfill criteria for diagnosis of MI according to Fourth universal definition of myocardial infarction (2018) [16].

Patients classified in to STEMI (44 patients) and NSTEMI (8 patients)

STEMI ST-segment elevation (measured at the J-point) 2.5mm in men < 40 years, 2mm in men > 40

Years, or > 1.5mm in women in leads V2–V3 and/or > 1mm in the other leads (in the absence of left ventricular (LV) hypertrophy or left bundle branch block LBBB) at least in two contiguous leads [17].

NSTEMI increasing and/or decreasing of a cardiac biomarker, preferably high-sensitivity cardiac troponin (hs-cTn) T or I, with at least one value above the 99th percentile of the upper reference limit with Symptoms of myocardial ischaemia or new ischaemic ECG changes(except persistent ST segment elevation > 20 minutes) [18].

- Age ≤ 65y (mean ages were 50.4 ± 8.2 years).
- They were 52 patients (38 males)

For Stroke patients

- Patients presented with acute ischemic stroke diagnosed according to world health organization criteria applied by a neurologist and confirmed by CT or MRI brain images or both [19].
- Patients classified according to TOAST classification [20] into large artery atherosclerosis (LAA) (46 patients) and small artery atherosclerosis (SAA) (5 patients):
- **LAA:** infarction in the perfusion territory of an extra cranial or intracranial artery with > 50% stenosis and no other likely cause of stroke [20].
- **SAA:** Imaging evidence of a single clinically relevant acute infarction less than 20mm in greatest diameter within the territory of basal or brainstem penetrating arteries in the absence of any other pathology in the parent artery at the site of the origin of the penetrating artery (focal atheroma, parent vessel dissection, vasculitis, vasospasm, and so on) [20].
- Age ≤ 65y (mean ages were 51.27 ± 7.6 years.
- They were 51 patients (36 males)

Exclusion criteria

For MI patients

- Patients above 65 years old.
- Patients with acute myocardial infarction not resulting from the atherosclerotic plaque, e.g. coronary artery spasm, embolism, coronary dissection or MINOCA.
- Patients who retrospectively diagnosed as non-myocardial infarction (alternative diagnosis e.g. takotsubo cardiomyopathy and myocarditis).
- Patients who was taking lipid-lowering drugs in 3 months prior to the study, which might affect the lipid metabolism

For ischemic stroke

- Patients above 65 years old.
- Patients who presented or retrospectively diagnosed as transient ischemic attack (TIA).

- Patients with haemorrhagic stroke.
- Patients with atrial fibrillation.
- Patients with intracardiac mass (tumor or thrombus).
- Patients with significant mitral stenosis.
- Patients with marked dilated left atrium.
- Patients taking lipid-lowering drugs in 3 months prior to the study, which might affect the lipid metabolism.

Study Design

This study was Observational cross sectional study

Sample size

(103) consecutive patients presented with acute MI (52 patients) even STEMI or NSTEMI and patients presented with acute ischemic stroke (non cardioembolic) (51 patients) and their ages were less than 65 y old, during the period from June 2020 to May 2022.**B-Operational Design**

1-Process

Selected patients were subjected to the following:

Full history taking

- Age and gender
- Risk factors for stroke and MI: hypertension, diabetes mellitus, family history for MI and stroke, CKD and smoking drug addiction.
- History for statin, antiplatelates, anticoagulant, contraceptive pills and other drugs.

Anthropometric measurements

- Weight in kilograms, height in meters, and body mass index (BMI).

Clinical examination include

- Blood Pressure.
- Pulse.
- General examination.
- Local cardiac examination.

Investigations include

- Laboratory measures: obtained by venepuncture within 2 hours after admission and delivered to the laboratory to perform:
- blood glucose and HbA1C
- Lipid profile (total cholesterol, LDL, HDL and triglycerides) Total cholesterol and triglycerides were measured in serum samples using enzymatic methods in an automated analyser (Hitachi, Roche-Diagnostics, Meylan, France). HDL-cholesterol was assayed by a direct technique, using polyanions/dextran and enzymatic reagents (Roche-Diagnostics). LDL- cholesterol was calculated using the Friedwald'sequation.
- Lipoprotein (a): its blood sample had been taken within 2 hours after admission and was frozen at −80 °C during the study duration, then measured by an immunoturbidimetric method, using a monospecific rabbit antiserum (Dako, Denmark) in an automated assay.
- hs-cTn I (using 0h/2h algorithm in NSTE-ACS patients for diagnosis of NSTEMI, according to ESC guidelines)[18].
- Renal function tests.
- 12 lead surface ECG.
- Echocardiography for all patients.
- Coronary angiography if done for MI patients.
- CT brain in stroke patients
- MRI and MRV in patients who suspected to have stroke mimics as Vasculitis.

2-Time line Patients who presented with acute MI or acute ischemic stroke (non cardioembolic) and their ages were less than or equal 65 y old during the period from June 2020 to May 2022 and their status fulfils the inclusion and exclusion criteria mentioned before.

3-Obstacles/limitations of study: Uncooperative patients who may refuse to give the consent of sharing in the study and the small sample size of this study.

C-Administrative Design

Approval of the institutional research board (IRB) and the medical ethics committee in Mansoura University had been obtained. All included patients will sign an informed consent for the study and for quality-control measures including echocardiographic examinations or additional cardiac imaging, and will receive a copy of these measurements along their medical reports on discharge. The patient will be also consented for publication of the clinical data while ensuring confidentiality of personal information.

Statistical Analysis

We reviewed the medical records for obtaining patients data and statistical data analysis had been done.

Descriptive data Descriptive statistics were calculated in the form of:

• Mean ± Standard deviation (SD)

• Median and range (Minimum-Maximum).

Analytical statistics

Data analyzed using Software SPSS version 26, Qualitative data were described using number and percent.

Statistical Analysis

Data were collected and submitted to statistical analysis. The following statistical tests and parameters were used.

Results

(**Table 1-4**), (**Figure 1**), (**Table 5**), (**Figure 2**), (**Table 6**), (**Figure 3**), (**Table 7**), (**Figure 4**), (**Table 8**), (**Figure 5**), (**Table 9**), (**Figure 6-8**).

Discussion

It was recognized that lipoprotein (a) (Lp (a)) concentrations were elevated in patients with cardiovascular disease (CVD). However, the importance of Lp (a) was not strongly established due to a lack of both Lp(a)-lowering therapy and evidence that reducing Lp(a) levels improves CVD risk. Recent advances in clinical and genetic research have revealed the crucial role of Lp

(a) in the pathogenesis of CVD.

Mendelian randomization studies have shown that Lp(a) concentrations are causal for different CVDs, including coronary artery disease, calcified aortic valve disease, stroke, and heart failure, despite optimal low-density lipoprotein cholesterol (LDL-C) management.

Lp (a) is a LDL-like particle synthesized in the liver, is known to be elevated in patients with CV events despite optimal LDL-C management. Lp (a) consists of Apo lipoprotein (apo) B100 covalently bound to apoA. Lp (a) characteristically inherits atherogenicity from both apoB and apoA, as well as prothrombogenic and proinflammatory traits from apoA. This collectively confers CVD-prone traits, unlike other lipoprotein particles that only have apoB These atherogenic, prothrombogenic, and proinflammatory traits led to the "Lp (a) hypothesis", namely that CV outcomes would be reduced by lowering Lp(a) concentrations.

The structural combination of apoB- containing LDL-C and apoA confers the superior atherothrombogenicity of Lp (a) over apoB-only LDL-C. The lysine-binding site of the kringle domains within an apoA molecule predisposes Lp (a) molecules to bind to the endothelial receptors, thereby contributing to atherogenicity. The structural homology of apoA to the plasminogen molecule also confers thrombogenicity of Lp(a). Therefore, an excess concentration of Lp (a) abrogates the function of plasmin activators, decreases plasmin levels, and eventually leads to attenuated fibrinolysis activity [6].

Although screening for Lp (a) is recommended by professional societies in selected patients, there is wide variation in the clinical utility of Lp (a) measurement among health care providers, and real-life data regarding the screening for Lp(a) levels in patients with established CAD is limited. Given its aforementioned

Table 1. Socio-demographic characteristics of the studied cases.

	Total number=103	%
Age/years Mean ± SD	50.7±7.9	
Sex		
Male	74	71.80%
Female	29	28.20%

Illustrates the mean age (±SD, in years) of the studied subjects was 50.7±7.9. Of the total number of the studied cases, 71.8% (n= 74) were males and 28.2% (n= 29) were females

Table 2. Medical history of the studied cases.

	Total number=103	%
DM	68	66
Smoking	66	64.1
Hypertension	62	60.2
BMI category Obese	29	28.2
Family history for AVSE	25	24.3
CKD	8	7.8

Shows demographic and medical history of the studied cases. Diabetes mellitus was recorded the highest percentage for 66% (n= 68), then smoking for 64.1%(n= 66), hypertension for 60.2% (n= 62), obese for 28.2% (n= 29), family history for premature AVSE for 24.3% (n= 25), CKD for 7.8% (n= 8).

Table 3. Laboratory and anthropometric measurements of all the study cases.

LP (a)	Mean(SD) Median(min-max)	28.71(19) 26.3(2-74)
LP categories (N, %)	Low High	60(58.3%) 43(41.7%)
LDL	Mean(SD) Median(min-max)	107.11(33.4) 100(46.3-200)
BMI	mean (SD)	27.6 ±4.2

Shows laboratory and anthropometric measurements of the study cases. Lipoprotein (a) (Lp (a)) ranged from 2 to 74mg/dl with median 26.3 and mean (SD) 28.71+19, Lp (a) (a) categorized to low < 30mg/dl and they were 58.3% (n=60) and high > 30mg/dl and they were 41.7% (n=43), LDL ranged from 46.3 to 200mg/dl with median 100 mg/dl and mean(SD) 107.11+33.4, BMI with mean(SD) 27.6+4.2.

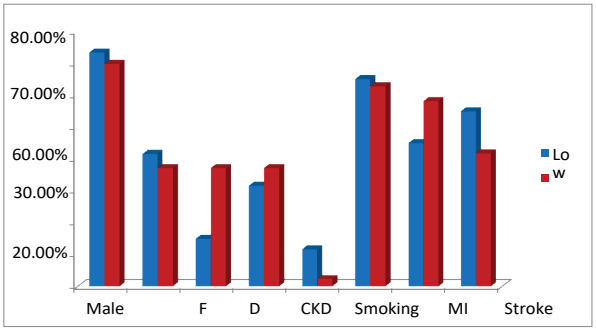

Figure 1 Comparison between LP (a) groups (low and high) and categorical data for all the study cases.

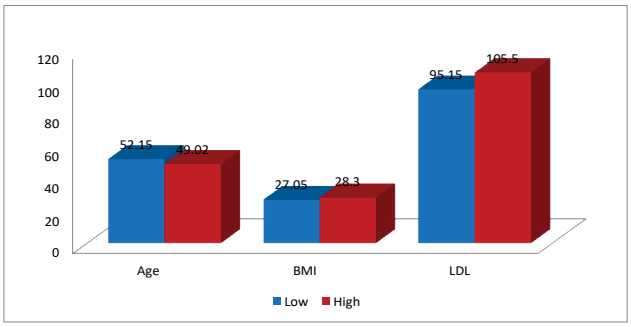

Figure 2 Comparison between LP (a) groups (low and high) and continuous data for all the study cases.

Table 4. Comparison between LP (a) levels and categorical data for all the study cases.

Categorical variables		LP (a) category			Test of OR 95% CI			
		Low	High		Significance			
		N=60	N=43			-	-	-
		N	%	N	%	-	-	-
Sex	Male	44	73.33%	30	69.77%	c2 =0.15	R	0.5-2.85
	Female	16	26.67%	13	30.23%	p= 0.69	1.19	
HTN		25	41.60%	16	37.21%	c2 =0.2		0.14-0.8
-	-	-	-	-	-	p= 0.64	0.8	-
FH of	premature	9	15.00%	16	37.21%	c2 =6.7	3.36	1.3-8.6
AVSE	-					p= 0.01*		
DM	-	19	31.67%	16	37.21%	c2 =0.34		0.56-2.9
	-					p= 0.55	1.3	
CKD	-	7	11.67%	1	2.33%	FET	0.18	0.02-1.5
	-					p= 0.13	-	-
Smoking	-	39	65.00%	27	62.79%	c2 =0.05	-	0.4-2
	-	-	-	-		p= 0.81	0.9	-
Subtype	NSTEMI	4	6.67%	4	9.30%	MC	-	-
	STEMI	23	38.33%	21	48.84%	P=0.4	-	-
	SAA	2	3.33%	3	6.98%		-	-
	LAA	31	51.67%	15	34.88%		-	-
AVSE	MI	27	45.00%	25	58.14%	c2=1.7	-	0.7-3.7
	Stroke	33	55.00%	18	41.86%	P=0.18	1.7 r	-

chi square , OR:odds ratio, FET: fischer exact test, MC:montecarlo test, r: reference group, CI: confidence interval *p value <0.05: significant

Shows comparison between LP (a) groups (low and high) and categorical data for all the study cases. In this table we noted that the percentage of family history for premature acute vascular ischemic event was higher in high level of Lp (a) patients than low Lp (a) patients (37.21%,15%) respectively, and it was statistical significant (P=0.01). Otherwise no significant difference between low and high Lp (a) groups as regard the other categorical variables.

Table 5. Comparison between LP (a) groups (low and high) and continuous data for all the study cases.

Continuous variables	LP (a) category		Test of significance
	Low N=60	High N=43	
Age	52.15 ± 6.7	49.02±9.1	T=2.49
	-	-	P=0.048*
BMI	27.05±4.3	28.3± 4.13	T=-1.4 p=0.14
LDL	95.15(46.3-190)	105.5(56-200)	Z=-1.8 p=0.06

T: independent t test Z: Mann Whitney test *p value <0.05: significant

Shows comparison between LP (a) groups (low and high) and continuous data for all the study cases. In this table we noted that the mean of ages was higher in low levels of Lp (a) patients than high levels of Lp (a) patients (52.15,49.02) respectively, and it was statistical significant (P=0.048). Otherwise no significant difference between low and high Lp (a) groups as regard the BMI and LDL.

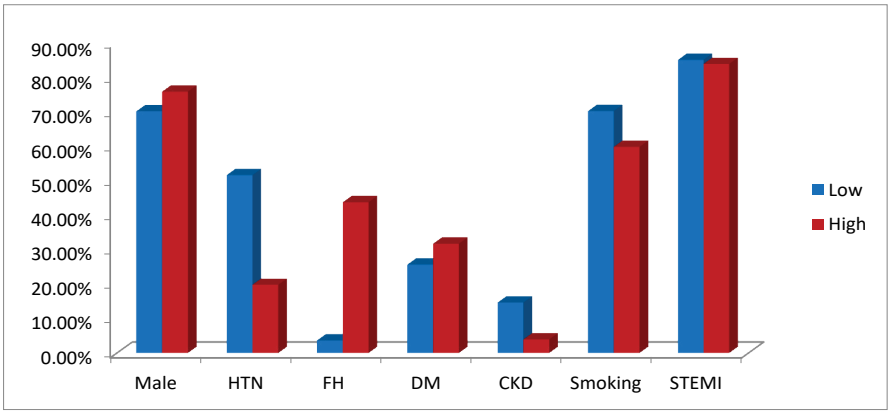

Figure 3 Comparison between LP (a) groups (low and high) and categorical data for MI cases.

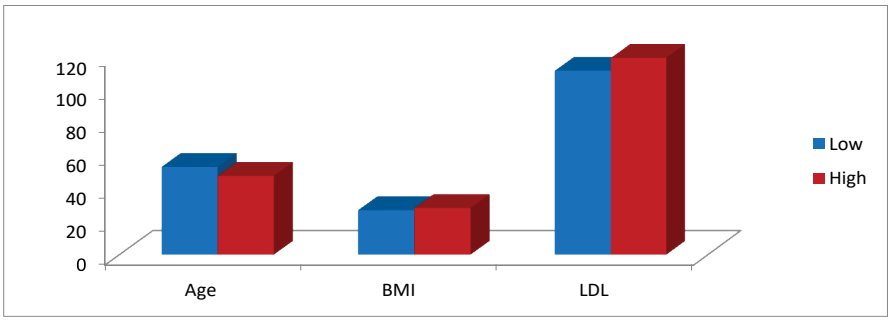

Figure 4 Comparison between LP (a) groups (low and high) and categorical data for MI cases.

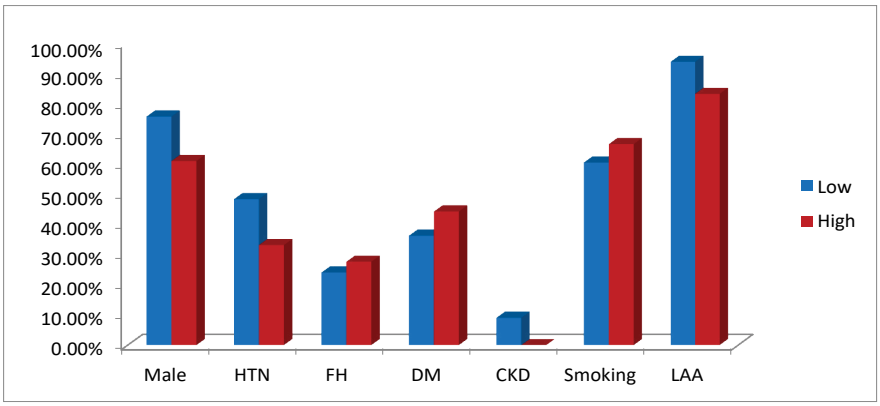

Figure 5 Comparison between LP (a) groups (low and high) and categorical data for Stroke cases.

Table 6. Comparison between LP (a) levels and categorical data among MI Cases.

		LP (a) category						
		Low N=27		High N=25		Test of significance	OR	95% CI
		N	%	N	%			
Sex	Male Female	19 8	70.30% 29.60%	19 6	76.00% 24.00%	c2 =0.2 p= 0.64	1.3 r	4-4.5
HTN		14	51.85%	5	20.00%	c2 =5.67 p= 0.017*	0.23	0.06-0.8
FH for premature AVSE		1	3.70%	11	44.00%	c2 =11.87 p= 0.001*	20.4	2.3-174
DM		7	25.93%	8	32.00%	c2 =0.23 p= 0.62	1.3	0.4-4.4
CKD		4	14.81%	1	4.00%	FET	0.2	0.02-2.3
Smoking		19	70.37%	15	60.00%	p= 0.35 c2 =0.61	0.6	0.2-1.9
Subtype						p= 0.43		
	NSTEMI STEMI	4 23	14.80% 85.20%	4 21	16.00% 84.00%	MC P=1	0.91	0.2-4.1

2:chi square OR:odds ratio FET: fischer exact test MC:montecarlo test r: reference group CI: confidence interval *p value <0.05: significant

Shows comparison between LP (a) groups (low and high) and categorical data for MI cases. In this table we noted that the percentage of hypertensive patients was higher in low level of Lp (a) patients than high Lp (a) patients (51.85%,20%) respectively, and it was statistically significant (P= 0.017). Also, family history for premature acute vascular ischemic event was higher in high level of Lp (a) patients than low Lp (a) patients (44%,3.7%) respectively, and it was statistical significant (P=0.01). Otherwise no significant difference between low and high Lp (a) groups as regard the other categorical variables.

properties, proactive screening of patients with MI and stroke (especially those with premature events or a family history) will be needed, with particular attention placed on the screening of individuals with recurrent events despite adequate lipid lowering, who frequently have high Lp(a) [8].

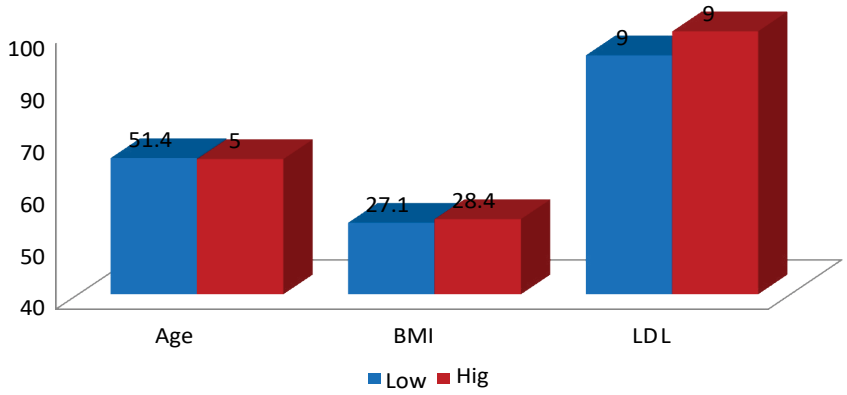

Figure 6 Comparison between LP (a) groups (low and high) and categorical data for Stroke cases.

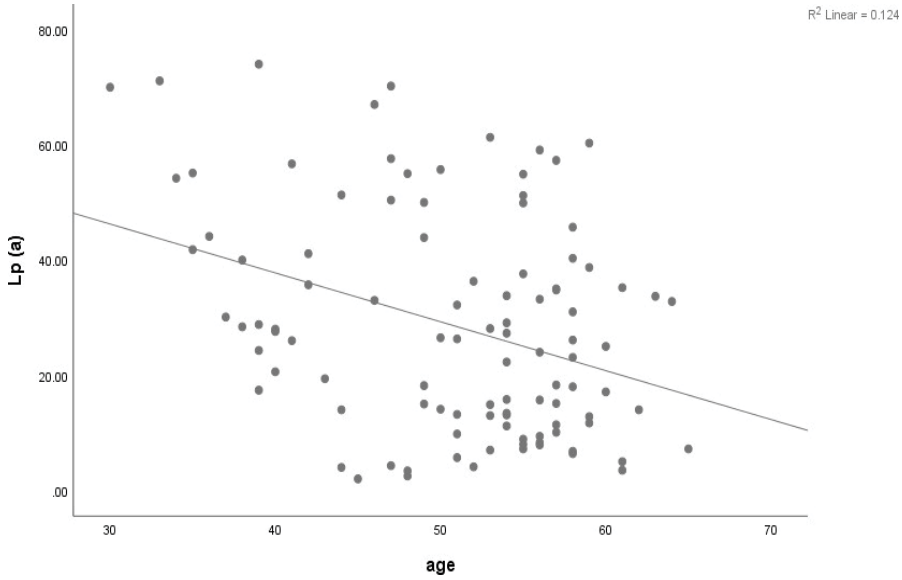

Figure 7 Correlation between LP (a) and age among study population.

Table 7. Comparison between LP (a) levels and continuous data among MI Cases.

	LP (a) category		
	Low	High	Test of significance
	N=27	N=25	
Age	53.04 ± 6.24	47.6±9.25	T=2.5 p=0.016*
BMI	26.96 ±4.6	28.2± 4.3	T=-0.99 p=0.32
LDL	111.2 ±30.88	119 ±31.21	t=-0.9 p=0.37

Little information is currently available on the utilization of Lipoprotein (a) as a screening measure in young and middle aged patients presented with acute vascular ischemic events. Therefore, it's critical to pinpoint the clinical traits, risk factors, and high-risk individuals that will be exposed to developing treatments and future preventive measures for raised Lp (a). Our study suggested Lp (a) as a possible predictor of Myocardial infarction (MI) and stroke in the Egyptian people.

Therefore, we conducted an Observational cross sectional study with the primary aim of this study sought to investigate Lp(a) in young and middle-aged patients ≤ 65 years presenting with acute myocardial infarction or acute ischemic stroke and evaluate its correlation to other risk factors for acute vascular ischemic event (AVSE). We hypothesized that elevated LP (a) levels would be associated with high incidence of AVSE in young aged patients especially with family history for premature AVSE.

Age, Socio-demographic data and their relation to other variables The mean ages of our patients was (50.7±7.9 years) as we were studying adult patients their age < 65years, similar to (52.2) ±8 years) in a study done by Jubran et al., 2019 that they were studying the same age category (adult < 65 years) while it was different to Colantonio et al., 2022 study that showed that the mean ages were around 68 years because they were studying Lp (a) in patients > 45 years with no upper limit.

Also, there was no significant difference between the mean ages for each group separately (MI and ischemic stroke) and it was (50.42 ± 8.22, 51.27 ± 7.6) Respectively, as the two diseases have

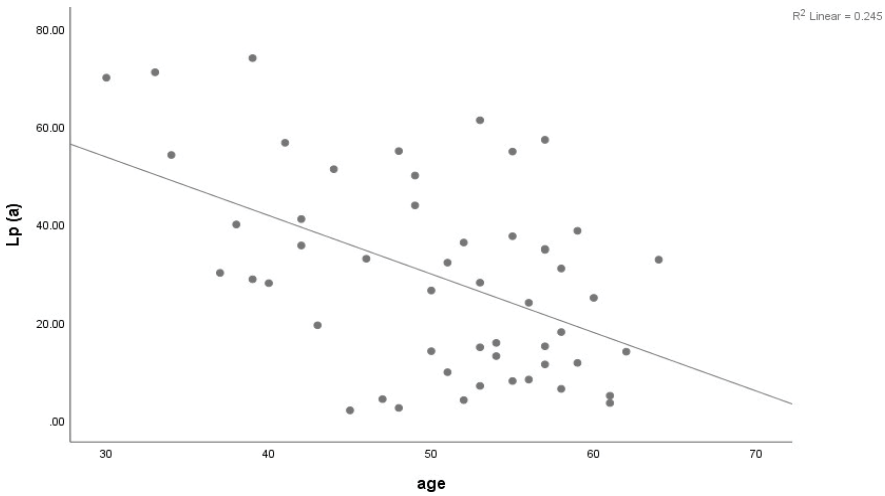

Figure 8 Correlation between LP (a) and age among MI cases N= 52.

Table 8. Comparison between LP (a) groups (low and high) and categorical data among patients with stroke.

		LP (a) category						
		Low (N=33)		High (N=18)		Test of significance	OR	95% CI
		N	%	N	%			
Sex	Male Female	25 8	75.80% 24.20%	11 7	61.10% 38.90%	c2 =1.2 p= 0.27	r 1.9	0.57-6.8
HTN		16	48.50%	6	33.30%	c2 =1.09 p= 0.29	0.53	0.1-1.7
FH for premature AVSE		8	24.20%	5	27.80%	c2 =0.07 p= 1	1.2	0.32-4.4
DM		12	36.40%	8	44.40%	c2 =0.31	1.4	0.43-4.5
CKD		3	9.10%	0	0%	p= 0.57 FET p= 0.3		
							-	
Smoking		20	60.60%	12	66.70%	c2 =0.18 p= 0.66	1.3	0.3-4.3
Subtype	SAA LAA	2 31	6.10% 93.90%	3 15	16.70% 83.30%	FET P=0.33	0.3	0.04-2.1

chi square FET: fischer exact test *p value <0.05: significant

Comparison between LP (a) groups (low and high) and categorical data for Stroke cases. In this table we noted that the percentage of , family history for premature acute vascular ischemic event was higher in high level of Lp (a) patients than low Lp (a) patients (27.8%,24.2%) respectively, but it was statistically non-significant (P=0.07). Otherwise no significant difference between low and high Lp (a) groups as regard the other categorical variables.

Table 9. Comparison between LP (a) levels and continuous data among patients with stroke.

	LP (a) category		Test of significance
	Low	High	
	N=33	N=18	
Age	51.42± 7.12	51 ± 8.77	T=1.87 p= 0.85
BMI	27.12 ±4.13	28.44± 4	T=-1.1 p=0.27
LDL	90(46.3-185)	99(56-169)	Z= -1.36 p= 0.17

T: independent t test Z: Mann Whitney test *p value <0.05: significant

Comparison between LP (a) groups (low and high) and continuous data for Stroke cases. In this table we noted that there was no significant difference between low and high Lp (a) groups as regard the age, BMI and LDL.

the age as strong risk factor.

Our study observed that the incidence of DM was more in middle aged patients (45:65 years) than young aged patients (ages <45 years), that is because the incidence of DM increases by age, and it had been proved by many studies for example Chandrupatla et al., 2020 demonstrate the same result in their study.

Our study showed that the median value of Lp (a) was higher in young aged patients than middle aged patients (32.9,22.3) respectively for all the study group, and it was statistical highly significant (P=0.006), several studies demonstrated the same results for example Choe el al., 1997 and Solfrizzi et al., 2009 showed that the value of Lp (a) is higher in young than the old aged patients presented with acute vascular events (MI, stroke, PAD).

But, in our study when we compared each group (MI and stroke) separately regarding Lp (a) and age categories, we observed that the median value for Lp (a) in MI patients was higher in young aged patients than middle aged patients (41.1, 18) respectively, and it was statistical highly significant (P=0.001) in comparison to stroke patients there was no significant difference between young and middle aged patient as regard Lp (a) levels.

Paré et al., 2019 demonstrated that the median value of Lp (a) was higher in young aged Myocardial Infarction(MI) patients than middle aged patients with MI and the difference was statistically significant (P=0.001) also Chung et al., 2021 noted that there is strong correlation between coronary calcification and high levels of Lp (a) in young aged patients.

Since 1996 there were some hypothesis that occurrence of ischemic stroke in young age mostly associated with high levels of Lp (a) and some cases were published since that date demonstrated those hypothesis, but most of the studies that had been done can't demonstrate the association between high levels of Lp (a) in young age more than middle or old aged patient with stroke, both of those study demonstrated that high levels of Lp (a) in stroke patients with no differences between age groups.

MI and stroke are still presented more frequent in male patients than female, in our study, male accounts as (71.8%), this result more or less was similar to findings by previous studies. (Rozenbaum et al., 2016), (Kurtul and Acikgoz, 2017).

In our study we classified our patients according to Lp (a) levels into high and low according to Canadian Cardiovascular Society Guidelines.

- High Lp (a): > 30mg/dl and they were 43(41.7%) patients
- Low Lp (a): < 30mg/dl and they were 60(58.3%) patients

The cut off value of Lp (a) for screening or to consider it high is not a point of convergence, ACC/AHA considered value (≥50 mg/dL) is a risk enhancing. also National Lipid Association considered (≥50 mg/dL) is a high value on the other hand Canadian Cardiovascular Society Guidelines considered > 30 mg/dl to be the high values.

In our study we selected (30mg/dl) to be the cut off value because

- Near to our mean and median values of our study and they were (28.7,263) respectively
- This value selected by most of the studies that was done on Lp (a)
- This value selected by Canadian Cardiovascular S o c i e t y Guidelines.

Lp (a) and AVSE

Our study showed that the prevalence of patients with high lp (a) is 43 cases and they resemble 41.7% from all the study cases, and it is consider high prevalence in comparison with the prevalence of high lp (a) (>30mg/dl) in general population that was 25% mentioned by Varvel et al., 2016 in their study.

The prevalence of high Lp(a) patients was 48% (25 cases) in MI cases in opposite to 35.2% (18 cases) in ischemic stroke, that predict that high Lp (a) is an independent risk factor for MI more than ischemic stroke.

In the same level of agreement with our study findings Jubran et al., 2019 retrospectively investigated the clinical features associated with elevated Lp(a) in young and middle-aged patients ≤ 65 years presenting with ACS. Their results indicated that, in young and middle-aged patient's ≤ 65 years of age presenting with ACS, previous revascularization and premature Coronary artery disease (CAD) were independently associated with elevated Lp (a), indicating progressive CAD and higher cardiovascular risk. In contrast, traditional cardiovascular risk factors were not associated with elevated Lp (a) and Plasma levels of Lp (a) are similar in men and women.

Similarly, Lisandro D. and his colleagues in their cohort study stated that, higher lipoprotein (a) levels are associated

With an increased risk for CHD events in Black and White adults with prevalent atherosclerotic cardiovascular disease (ASCVD). There was no evidence of an association between lipoprotein (a) and ischemic stroke events among Black or White participants.

Moreover, High Lp(a) concentration was associated with MI , and in different ethnic subgroups with arrange of mean Lp(a) levels, except Arabs (with relatively low mean levels) and Africans (with the highest levels). However, these 2 ethnic groups had the smallest sample size in this study. Collectively, these observations point toward a role for Lp(a) concentration in MI risk stratification, and to important differences with respect to population distribution in Lp(a) concentration.

Conversely, Lipoprotein (a) was not found to be significant predictor for Acute vascular ischemic event (both MI and stroke) by the same level, but we found a higher levels of lipoprotein (a) associated with the increase the risk of MI more than stroke, in the same direction Lasiandra's study results reported no association between lipoprotein (a) and ischemic stroke events.

Anne Langsted and her colleagues: carried out a study to test if high lipoprotein is associated with high risk of ischemic stroke observationally and causally from human genetics. Their results reported that very high plasma levels of lipoprotein (a) were associated with increased risk of ischemic stroke both observationally and causally from human genetics.

Also, a meta-analysis study performed by Alexander. H and his colleagues, their results were collaborated with Anne's study findings. They stated that, Elevated Lp (a) is an independent risk factor for ischemic stroke and may be especially relevant for young stroke patients.

There are several possible explanations for differences in the study's results regarding association between Lp (a) and ischemic stroke including:

- Different mechanisms of ischemic stroke (cardio embolic, non-cardio embolic) that not differentiated in most of the studies
- Differences in the study populations.
- Differences in the study endpoints

- Differences in the study methodologies of Lp (a) measurement. Among them.
- Race-based differences in Lp (a) levels and the relationship between Lp(a) and cardiovascular disease could have major effects. It is well- documented that individuals of African descent have two- to three- fold higher Lp (a) levels than Caucasian individuals.

Furthermore, predictive values and cut-off points of Lp(a) for cardiovascular events and stroke might be influenced by race/ethnicity. Most of the previous studies that investigated the prognostic utility of on- treatment Lp(a) enrolled only white participants.

Lp (a) and FH for premature AVSE

The current study found that the percentage of family history for premature acute vascular ischemic event was higher in high levels of Lp (a) patients than low Lp (a) patients (37.21%, 15%) respectively, and it was statistical significant (P=0.01) these findings were in accordance with Jubran's study findings, and these result support the hypothesis that Lp (a) is genetically determinant, and strongly associated with FH.

Conclusion

Young and middle aged patients < 65y years presented with acute vascular ischemic event (MI and stroke) were independently associated with elevated Lp(a), especially in patients with MI, young aged and with FH for premature acute vascular ischemic event.

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