Lipoprotein(a) and lipid profile in Añú Ethnicity residents of the Sinamaica Lagoon, in the Páez district, Zulia State – Venezuela

Bermúdez Valmore, MD, MPH, PhD., Siciliano Adriana, MD., Acosta Luis, MD., Rojas Edward, MD., Aparicio Daniel, MD., Finol Freddy, MD., Canelón Roger, MD., Mengual Edgardo, MD., Rojas Joselyn, MD.
"Dr. Félix Gómez" Endocrine-Metabolic Research Center. Zulia University. Medicine Faculty. Maracaibo, Venezuela.
Author Correspondence: Valmore Bermúdez, MD; PhD. Zulia University, Medicine Faculty. "Dr. Félix Gómez" Endocrine-Metabolic Research Center.
E-mail: ciemfelixgomez@gmail.com; sefiem_ciem@hotmail.com

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Abstract

Introduction: Lipoprotein(a) [Lp(a)] has been associated with ischemic arterial disease and varies according to the ethnic origin of the studied populations. In our country, and especially in Zulia state, very few trials have been realized analyzing Lp(a). In light of this, the purpose of this investigation was to determine levels of Lp(a) in the Añú population from Zulia State – Venezuela, and evaluate the possible relation as morbidity and mortality factor in this genetic homogenous population. Materials and Methods: A cross-sectional study was undertaken, randomly selecting 120 patients from both sexes, beyond 18 years of age, from the Añú population localized around the Sinamaica Lake in the Páez Distric, Zulia State – Venezuela. A complete medical history was obtained, and after an 8 -12 hours fast, an antecubital venous blood sample was taken. Results: Lp(a) in the studied population was 13,3 mg/dL, with a mean value for women of 11,8 mg/dL and men of 15 mg/dL. The 10th, 50th and 90th percentile were 3,2 mg/dL,13,3 mg/dL and 53,1 mg/dL respectively. Conclusion: Low Lp(a) concentrations observed in the Añú populations are similar to the concentrations observed in other Indigenous groups from North America and Japan. We propose that Lp(a) is not determinant for the occurrence of acute cardiovascular events or cerebrovascular disease in indigenous populations. It is necessary to conduct cohort and prospective studies to refute or prove our findings.

Keywords: Lipoprotein(a), cardiovascular risk factor, ethnicity, Venezuela indians

Introduction

Venezuela, and particularly the Zulia State, have the privilege of having a vast ethnic diversity; it`s considered a fishing zone, being this the main source of food, acquiring this trait from the Spanish Colonists. The Natives groups can be described from Amerindians in the Perijá Mountain Range represented by the Barí and Yucpa groups, and more to the north, in the Guajira Peninsula with groups Wayúu and Paraujano or Añú. To the south of Maracaibo Lake, there are Afroamerican populations in the Sucre District, such as San José de Heras, Santa María and Bobures. According to the epidemiological reports, the main cause of death in these parts of the state is heart disease[1].

Añú population is located around the Sinamaica Lagoon (Figure 1), and it's divided into 15 sectors: El Barro, La Boquita, Las Parcelas, Nuevo Mundo, Caño Morita, El Cañito, Puerto Cuervito, El Junquito, Boca del Caño, La Ponchera, Zanzíbar, Lagunita, El Javal, La Rosa, and Brasil Island. They are characterized by a typical over water housing structure called "palafitos" (Palafittes)[2-3]. These ethnic groups have been subject to westernization, due to the introduction of industrialized foods and transportation very different to their standard rowing canoes, which in combination with an elevated analphabetism index and genetic makeup, provide a primordial broth that ends up in the developing of chronic degenerative diseases; among them, obesity, diabetes and metabolic syndrome[4-6].

Parallel to the ongoing situation in the occidental world, coronary artery disease (CAD) is the leading cause of mortality in Venezuela, with 24,977 deaths (20,63%) according to the Mortality Year Book in 2006. In order of

importance, these are the most frequent diagnosis: Acute Myocardial Infarction (12,70%), Hypertensive Cardiac Disease (2,46%) and Chronic Ischemic Myocardial Disease (2,19%)[7]. A similar behavior can be seen in the Zulia state, where the Cardiovascular Diseases (CVD) are the first cause of mortality, with a rate of 107.47 per 100,000 habitants. Likewise, in the Páez district (belonging to this state), CVD are the main cause of death with a rate of 62.63 per 100,000 habitants[1].

If one studies the physiopathology of these diseases, a tight relation can be observed between CAD, Atherosclerosis and Cardiovascular mortality. Half of the patients with CAD have lipoprotein metabolism abnormalities and this shines light on some risk factors like excess weight, life style, alcoholism, smoking habits, high saturated fatty acid intake and genetic susceptibility[8-10]. The relationship between lipid alterations and morbimortality due to cardiovascular events has been demonstrated with pathology and biochemical evidence, and dyslipidemic influence can be appreciated in the atherogenic and thrombotic process that leads to arterial obstruction[11].

A lot of studies point to a relationship between Lipoprotein(a) [Lp(a)] and ischemic arterial disease, but not all[10,12]. In the same manner, a good share of researches show that elevated concentrations of Lp(a) and increased incidence of cerebrovascular disease, CVD, reestenosis of coronary bridges, re-occlusion in angioplasty procedures due to premature atherosclerotic and thrombotic phenomena, alongside lipid alterations like high low density lipoproteins (LDL-c) and low high density lipoprotein (HDL-c)[13-14].

Lp(a) concentration varies according to each ethnic group of origin studied. It is highly asymmetric and teds to be low in Caucasians and Asians, and tends to be elevated (but less asymmetrical) in Blacks and Afroamericans[15].

It has been recently proposed that in the assembly process, size of the apoprotein (a) [apo(a)] matters. It`s been known for quite a long time that the size of apo(a) is variable form one individual to another, identifying 34 isoforms of apo(a) so far[12]. These differences are associated with higher risk for premature atherosclerosis. The big isoforms are associated with low levels of Lp(a) – as in Caucasians – and, on the contrary, small isoforms are correlated with high levels of Lp(a) – as in Black individuals[16].

In South America very few studies have been focused on Lp(a) levels even less in Indian groups so the purpose of this investigation was to determine levels of Lp(a) in the Añú population from Zulia State – Venezuela. And in the same manners, evaluate its possible relation as a morbidity and mortality risk factor in cardiovascular disease in this homogeneous genetic population.

Materials and methods

Population

A cross-sectional study was undertaken on individuals of both sexes (Female: 102; Male: 35), born and resident in Sinamaica Lagoon in the Páez district, Zulia State–Venezuela with family ancestry Añú verified by means of interrogation. According to the Census of Indigenous Communities 2001[17], Añú ethnicity in Venezuela is comprised de 11205 individuals (2,3% of the national indigenous population), of which 3854 live in traditional communities and the remaining 7351 residents in urban communities. Traditional community that keeps alive the culture Añú is settled in the lagoon. The last census conducted there show little increase in population during the past 50 years, by 2000 there were only 3481 inhabitants located in 538 homes.[18] The population estimated of Sinamaica Lagoon in the Páez District, Zulia State–Venezuela for the 1º of July, 2008 belong 4.000 habitants, of which approximately 50 % corresponds to adult population (2.000 habitants) there being estimated a sample size of 137 adults individuals. The method for the selection of this sample randomly, chosen by drawing 5 housings in every sector of Sinamaica's Lagoon.

A complete medical history was performed, and after 8 – 12 hours fasting period, an antecubital venous sample was drawn and serum was obtained after 10 minutes centrifugation at 4.000 R.P.M. Lp(a) determinations were done using the turbidimetric latex test (Human Gesselschaft für Biochemica und Diagnostica mbH, Germany)[19]. This method detects the presence of Lp(a) using latex agglutination of particles coated with anti-Lp(a) antibodies. This agglutination is proportional to the concentration of Lp(a) in the sample, and it can be measured by turbidimetry.

In relation to lipid profile, for the determination of total cholesterol, LDL-c and triglycerides was used the direct enzymatic method (Human Gesellschoft Biochemica and diagnostica MBH), HDL-c concentrations were measured with the precipitation method (Human Cholesterol Liquicolor Test Kit) and the values of the cholesterol VLDL were obtained by means of the subtraction to the value of the total cholesterol of the rest of the lipidic fractions.

Statistical Analysis

For the statistical analysis, SPSS (Statistical Package for the Social Sciences) for Windows version 15.0 was used. The normal or not normal distribution of the variables was proved using the Kolmogorov-Smornov Z test. For the normal distribution variables, the results were expressed in mean arithmetic ± standard deviation, and the differences between them was established applying Student t test (when two groups were compared) or ANOVA for one factor and post hoc Tukey test (when comparing three or more groups). For the not normal distribution variables, the results were expressed in averages, and the differences between them were evaluated using the Mann-Whitney U test, considering $p<0,05$ as a statistically significant.

In Table 1, the clinical characteristics of the Añú individuals are presented. Overweight was observed, with an average body mass index of 27,2±6,0 kg/m^2 (Female: 26,3±0,6 kg/m^2, Male: 29,9±1,0 kg/m^2; p=0,002) and a mean abdominal perimeter of 89,6±15,4 cm (Female: 85,4±13,7 cm, Male: 101,7±13,9 cm; p=0,001).

Median for systolic arterial pressure (SAP) was 120 mmHg (Female: 115 mmHg, Male: 130 mmHg; p=0,001) and for the diastolic arterial pressure (DAP) 80 mmHg (Female: 80 mmHg, Male: 90 mmHg; p=0,001). Using the blood pressure values, the population was categorized in pre-hypertension (36%), hypertension state I (14,7%) and hypertension state II (19,9%) using the Joint National Committee classification[20] (JNC-VII).

When the plasmatic lipids were analyzed the mean of HDL-c was 39,2±10,6 mg/dL showing that 79,4% had low HDLc and the male patients had lower HDL-c compared with the female patients (Female: 40,8±10,6 mg/dL, Male: 34,5±9,1 mg/dL; p=0,001), the rest of means of the others parameters were a normal mean, using the values proposed by the NCEP Adult Treatment Panel III[21]. The median of glycemia was 85 mg/dL (Female: 84 mg/dL, Male: 91 mg/dL; p=0,003). (Table 2).

Distribution of the Lp(a) variable was normal. Lp(a) concentration in the population was 13,3 mg/dL, with a mean of 11,8 mg/dl for the females and 15 mg/dL for males, not observing any significant difference (Figure 2). The 10th, 50th and 90th values were 3,2 mg/dL, 13,3 mg/dL and 53,1 mg/dL, respectively.

No significant differences were observed in the levels of Lp(a) in the Añú patients comparing them according to age and sex (Figure 3). Likewise, no difference was observed when analyzed according to family cardiac disease history (Figure 4).

Table 1. Clinical characteristi

	Female	Male	Total
n	102	35	137
Age (years)	37,5±13	40,5±13	38±13
Weight (Kg)	62,4±1,5	81,6±3,0*	67,3±17,8
Height (Meters)	1,54	1,65*	1,55
Body Mass Index (Kg/m^2)	26,3±0,6	29,9±1,0**	27,2±6,0
Abdominal Perimeter (cms)	85,4±13,7	101,7±13,9*	89,6±15,4
Blood Pressure Values (mm Hg)			
SAP	115	130*	120
DAP	80	90*	80

Table 2. Glycemia and Lipid Profile in the Añú patients according to sex cs of the Añú patients according to sex.

	Female	Male	Total
n	102	35	137
Glycemia (mg/dl)	84	91¥	85
Total Cholesterol (mg/dl)	171,2±36,5	188,6±37,8*	175,6±37,5
Triacylglycerides (mg/dl)	89,5	139**	97
HDL-c (mg/dl)	40,8±10,6	34,5±9,1ɣ	39,2±0,9
LDL-c (mg/dl)	109,6±31,8	121,1±32,7	112,6±2,8
Non-HDL Cholesterol(mg/dl)	130,3±37,4	154,1±34,3α	136,4±3,2
VLDL-c (mg/dl)	20,6±11,6	33,0±17,7**	23,8±14,4

Figure 1. Zulia State.

		Lp(a) Levels [mg/dl]	Lp(a) Levels [mg/dl]	Lp(a) Levels [mg/dl]
		Female	Male	Total
n		102	35	137
Mean±S.E.		20,7±2,7	27,3±5,6	22,4±2,5
Mean		11,9	15,0	13,3
Minimum		0,5	3,1	0,1
Maximum		183,0	190,3	190,3
Percentil	10	3,1	3,4	3,2
Percentil	50	11,9	15,0	13,3
Percentil	90	51,5	55,6	53,1

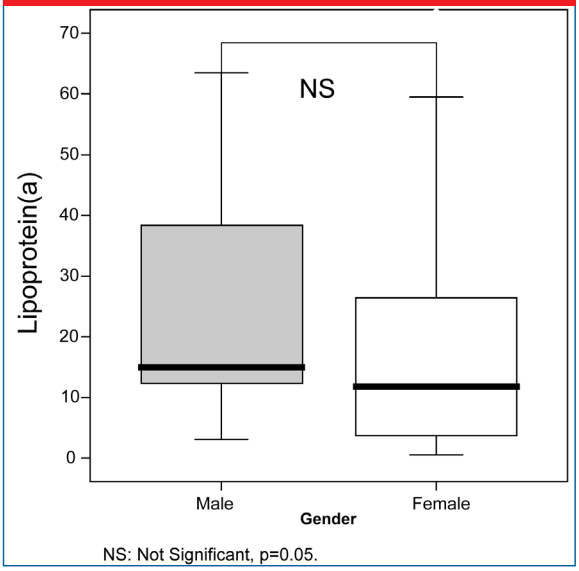
Age groups (years)	n	Mean±S.E.
18-29	38	20,7±4,0
30-39	42	23,5±4,9
40-49	33	26,4±6,2
50-59	16	19,3±5,8
≥60	8	14,1±5,2
Total	137	22,4±2,5

History CVD	n	Lp(a) [mg/dl]
With	86	25,0±3,5
Without	51	17,8±3,2

Table 3. Lipoprotein(a) Concentration in Genetically Diverse Populations

Population or Ethnos	n	Findings	Reference
635 boys and 648 girls from Taipei, from 12 to 16 years	1283	Median of serum Lp(a) levels were 8.8 mg/dl in boys and 11.9 mg/dl in girls. Lipoproteins profile rather than anthropometric measures, are significantly associated with serum Lp(a) levels among school children.	30
30 men and 30 women from each ethnic group (Koreans, Chinese, Tibetans, Nigerians, and Belgians)	300	The median lipoprotein(a) levels in Koreans, Chinese, Tibetans, Nigerians, and Belgians were 99, 89, 49, 134, and 80 mg/liter, respectively	15
233 Individuals from Maywood, IL (USA) a Black Working Community and 252 from Ibadan, an indigenous city in Nigeria	485	Mean serum Lp(a) values were significantly higher in the United States than in Nigeria (20.5 vs. 12.7 mg/dl; p= 0.0001) and U.S. blacks had a higher frequency of the large molecular weight isoforms compared to Nigerians.	31
African-Venezuelan populations from South of Maracaibo´s Lake: Bobures (n = 55), San José de Heras (n = 109) and Santa María (n = 147)	311	Median of Lp(a) concentration were unusually high (Bobures: 59.00mg/dL; Santa María: 47.00mg/dL; San José: 41.00mg/dL) and are even higher than those reported previously in other black populations of USA and Africa	27
American Indians from 13 communities in Arizona, Oklahoma, and South/North Dakota	3991	Median of Lp(a) concentration was 3.0 mg/dl. Correlation analysis showed Lp(a) was significantly negatively correlated with the degree of Indian heritage and is not an independent predictor of CVD among American-Indians.	28
865 Japanese and 1893 Dominican apparently healthy subjects	2758	Mean Lp(a) concentration in Dominicans was approximately 2 times higher than Japanese (21,7 ± 23,7mg/dL vs. 12,3 ± 15,9mg/dL; p<0,001).	29
25 men and 25 women (age range: 23-75 years) who had migrated to Australia from India over the past 20 years	50	Mean Lp(a) value in this group of Asian Indians was 32.5 mg/dL, a value higher than that reported in most other studies	32
Tyrolean (n=279), Icelandic (n=184), Hungarian (n=202), Malay (n=125), Chinese (n=112), Indian (n=143) and Black Sudanese (n=105)	1150	Mean Lp(a) in Tyrolean was 14,1 ± 19,4mg/dL, Icelandic 45,7 ± 25,9mg/dL, Hungarian 8,3 ± 11,0mg/dL, Malay 12,9 ± 17,9mg/dL, Chinese 7,2 ± 13,1mg/dL, Indian 20,1 ± 15,9mg/dL , Black Sudanese 45,7 ± 25,9mg/dL	33
Group 1, 57 subjects living in India and diagnosed with CHD. Group 2, 46 healthy subjects living in India. Group 3, 206 Asian Indians living in USA.	309	Lp(a) mean in Group 1 was 12.65 ± 9.40mg/dL, in Group 2 was 9.15 ± 7.33mg/dL and in Group 3 was 8.67 6 ± 8.24mg/dL. Elevated Lp(a) levels confers genetic predisposition to CHD in Asian Indians, and nutritional and environmental factors further increase the risk of CHD.	34
71 white and 41 Pehuenche Indians from Chile from 6 to 15 years old.	112	Mean of Lp(a) levels for Pehuenche and Caucasian children were 10.5 ± 6.2 and 21.3 ± 34.5 respectively (p < 0.001), so the firsts have probably less cardiovascular risk as far as Lp(a) serum levels are concerned.	35
137 subjects apparently healthy from Maracaibo City and 47 subjects from Casigua el Cubo, Zulia State – Venezuela.	184	Median Lp(a) concentration in Maracaibo (white population) was 29 mg/dl, and in Casigua el Cubo (mixed population) was 30 mg/dl.	36
African-Americans (n = 47), Native Americans (n = 45) and Caucasians (n=48) women with 40-70 years old in a physical activity program	140	Median Lp(a) concentrations were 28.3 mg/dl (25-75%: 10.4-43.1 mg/dl) in African-Americans, 2.9 mg/dl (25-75%: 1.2-7.4 mg/dl) in Native Americans, and 9.4 mg/dl (25-75%: 2.6-22.4 mg/dl) in Caucasians. Physical activity and maximal treadmill time did not influence Lp(a) concentrations.	37
Three Native Mexican populations [Mayos (n= 68), Mazahuas(n= 60) and Mayas (n= 36)] and in Mestizo subjects (n=41)	205	Mestizos presented the less skewed distribution and the highest Lp(a) median (13.25 mg/dL) relative to Mazahuas (8.2 mg/dL), Mayas (8.25 mg/dL) and Mayos (6.5mg/dL). Phenotype distribution was different in Mayas and Mazahuas as compared to the Mestizo group.	38
3484 residents (53% women; age range, 35-97 years) in the Chin-Shang Community, a suburb of Taiwan followed for 13.8 years	3484	A threshold relationship, with little gradient of risk for stroke and all-cause death across Lp(a) values among Chinese individuals.	39

Figure 2. Levels of Lp(a) in the Añú patients according to sex



NS: Not Significant, p=0.05.

Figure 3. Lp(a) levels in Añú patients according to age.

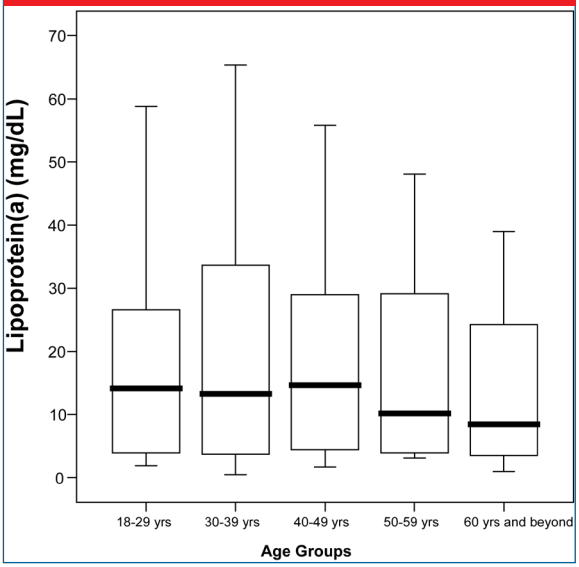
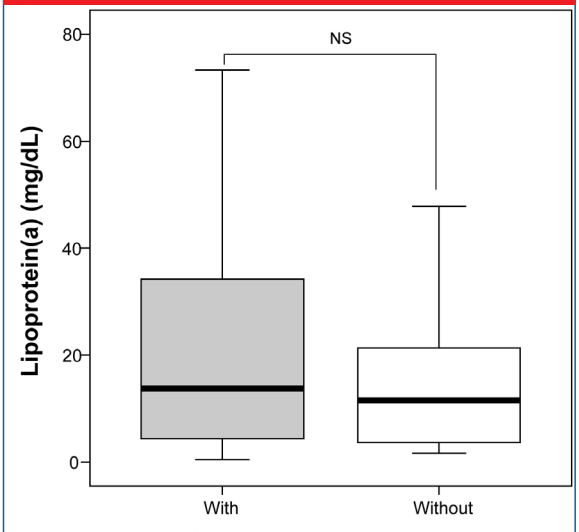


Figure 4. Lp(a) serum levels in Añú patients according to cardiac disease family history.



NS: Not Significant

Discussion

Even though not all the studies can demonstrate that extreme Lp(a) levels predispose to acute coronary events[22-23], Kamstrup et al. conducted a prospective study using 9,330 individuals, showing that patients with extreme Lp(a) concentrations (≥120 mg/dL) had 2 – 4 fold risk for a Myocardial Infarction within 10 years. In this study, the mean levels of Lp(a) in the studied population was much lower compared to other populational studies like the one conducted by Braeckman et al.[24] in Belgium, where the levels of Lp(a) were analyzed in workers, with mean values of 23,1 ± 9 mg/dL.

Similar results those of Braeckman et al. published Donders et al.[25] in 1992. Observing Lp(a) mean values according to sex, it is noteworthy that not a single one of the females had Lp(a) levels over 30 mg/dL (normal cut-off level), comparing with other studies that have showed maximum values of 225 mg/dL.

When analyzing levels of Lp(a) using CVD family history, it was observed that the ones with the highest levels of Lp(a) (25 mg/dL) has no previous family history, compared to those with lower levels (17,8 mg/dL) and with a positive CVD background. These findings do not match other results from previous trials where those with family history had higher levels of this lipoprotein. One of these trials, is the Copenhagen Heart Study[26] that establishes that high levels of Lp(a) are a risk factor for CVD.

Little documentation exists globally and especially in South America on studies that assess levels of Lp(a) in different ethnic groups mainly indigenous and afrodescendent (Table 3). Differences between Lp(a) concentrations between our Añú group and the groups from the south of the Maracaibo Lake – whom derive from the Sub-Saharan Africa populations – are shocking. The Bobures population had Lp(a) levels of 50,00 mg/dL, Santa María had 47,00 mg/dL and San José de Heras had 41,00 mg/dL, showing significant differences when compared to each other: Bobures vs Santa María with p=0,009, and, Bobures vs San José de Heras with p=0,02[27].

In a similar study as our own, but on a bigger scale (n=3,991), a prospective research was conducted in North American Natives from Arizona, Oklahoma, North and South Dakota, reveling that the concentrations of Lp(a) were considerably lower (3 mg/dL), and ergo, Lp(a) levels are not predictors of acute cardiovascular events in these populations[28].

The concentrations observed in our Native group concur with the ones Aono et al.[29] published studying the Japanese populations. In this research, the levels of Lp(a) from Dominicans and Japanese were compared finding significant differences (21,7 ± 23.7mg/dL vs. 12,3 ± 15,9mg/dL; p<0,001).

Conclusion

Taking into consideration all that has been explained, we can propose that Lp(a)'s role in acute cardiovascular events and cerebrovascular disease is not definitive in aborigines populations; yet, its participation in Caucasians and Afroamericans indicates the contrary. So, it is really necessary to conduct cohort and prospective studies that evaluate the incidence of acute cardiovascular and cerebrovascular diseases with Lp(a) concentrations in aboriginal populations.

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