

Epidemiological Study of Lipoprotein (a) in Okinawa

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A study of serum levels of lipoprotein (a) (Lp (a)) was performed among 217 normal adults including 135 men and 82 women in the northern part of Okinawa. Ages of the subjects ranged from 24 to 76 with an average of 49 years. Concentrations of Lp (a) in blood were measured by sandwich ELISA. The average Lp (a) concentration was 20.7 mg/dl and the peak of the distribution of serum Lp (a) concentration ranged from 10 to 15 mg/dl. A greater number of people in the investigated area tended to show a higher level of serum concentration of Lp (a) than those in any other prefectures in Japan, although there was no significant relationship between serum level of lipoprotein (a), total cholesterol, triglyceride, age or gender in healthy subjects.

Key words : lipoprotein (a), total cholesterol, triglyceride

Introduction

Lipoprotein (a) is a glycoprotein discovered by Berg et al. (1) in 1963 and is supposed to be a lipoprotein which contains apolipoprotein (a) linked by a disulfide bond to apolipoprotein B (2). Blood concentration of Lp (a) is genetically regulated, and is not affected by age, gender, or environmental factors. It is known that the frequency distribution pattern of Lp (a) concentration differs in race, and the concentration is a clinical risk factor for atherosclerosis and ischemic heart disease

People of Okinawa enjoy greater longevity than people of other prefectures in Japan. The mortality rate due to ischemic heart disease or cerebrovascular disease is remarkably lower in this prefecture (3). To determine the cause, studies concerning various factors such as nutrition, environment, and so on, have been performed. However, the data on Lp (a) has not yet been reported to our best knowledge. We performed an epidemiological study by measuring serum Lp (a), choosing people from one area of Okinawa as the subjects. Data along with its evaluation are presented in this report.

Materials and Method

The subjects consisted of normal 217 adults, including 135 men and 82 women, undergoing a routine medical check-up in a locality in northern Okinawa. Ages of these people ranged from 24 to 76 years and the average age was 49 years. Fasting blood was collected from the objects early in the morning. GOT, GPT, r-GTP, alkaline phosphatase (Al-P), total protein, albumin, total cholesterol, and triglyceride were measured biochemically. The sera for Lp (a) measurement were collected in inheritant examinations and stored at -40°C . Lp (a) concentration was measured by sandwich ELISA method (tintELIZE Lp (a), Cosmo-bio Co., Inc. Tokyo).

Briefly, we reacted anti-apo (a) solid-phase antibodies with 20 microliters of a diluted sample made by mixing 1 ml of the dilution buffer with 20 microliters of the serum. After washing, peroxidase-conjugated anti-apo (a) antibodies were added, reacted, and antigen-antibody complexes were formed. Then, after rewashing, hydrogen peroxide and o-phenylene diamine were added. Finally, the degree of luminescence was measured at 492 nm.

Result

1) General frequency distribution of serum Lp (a) concentration : Figure 1 shows the frequency distribution of serum Lp (a) concentration of normal adults living in

Table 1 Mean value of Lp (a) by age and sex

Age	No. Tested	Male	Female	Total
20-29	7	11.9 \pm 2.7	12.2 \pm 5.0	12.0 \pm 3.0
30-39	40	19.6 \pm 42.7	16.1 \pm 7.3	18.3 \pm 35.0
40-49	67	18.5 \pm 18.2	30.9 \pm 47.5	23.5 \pm 33.5
50-59	59	23.4 \pm 28.0	17.5 \pm 9.5	22.1 \pm 25.2
60-69	29	25.0 \pm 22.7	14.2 \pm 11.6	19.7 \pm 18.7
70-	15	14.9 \pm 18.5	14.8 \pm 10.4	14.8 \pm 12.3
Total	217	20.7 \pm 27.5	20.6 \pm 29.6	20.7 \pm 28.3

Data are expressed as mean \pm standard deviation

Table 2 Comparison of clinical data between low and high Lp (a) groups

	Age	M/F	T.chol.	TG	GOT	GPT	r-GTP	Al-P
Low Lp (a) group (n=176)	49.2±12.0	1.6	206.6±37.5	132.3±74.8	22.8±9.7	27.1±16.4 ^{**}	29.2±32.6 [*]	143.8±39.4
High Lp (a) group (n=416)	49.9±10.1	1.9	215.4±31.7	125.3±78.3	21.1±5.4	21.5±7.0	21.2±17.4	135.6±30.7

Figures indicate mean value except for male female ratio
 T. chol : Total cholesterol, TG : Triglyceride, Al-P : Alkaline phosphatase
 * : P<0.05, ** : P<0.01
 Data are expressed as mean ± standard deviation

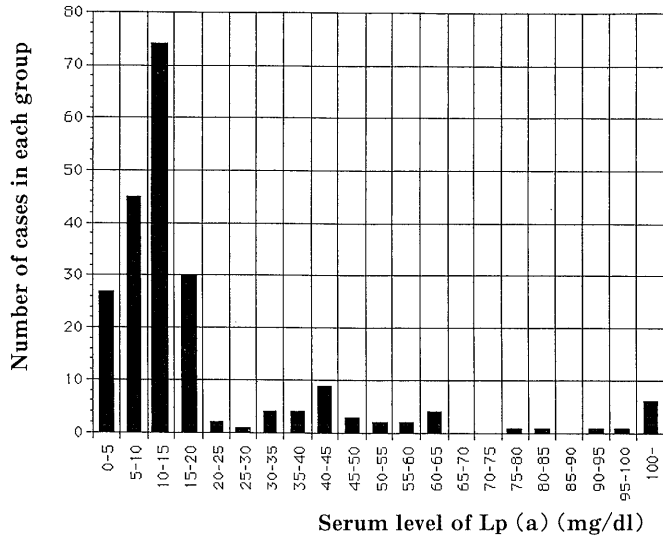


Fig. 1 Frequency distribution of serum Lp (a) level in 217 cases

northern Okinawa. The total average value of serum Lp (a) was 20.7 mg/dl and it was higher than any other report in Japan. The peak of frequency distribution of the Lp (a) concentration ranged from 10 to 15 mg/dl. There was also another weak peak between 40 and 45 mg/dl.

2) Differences in serum Lp (a) concentration by age and gender : Mean value of serum Lp (a) level of different age groups is presented in Table 1. The average serum concentrations of Lp (a) for males and females were almost the same at 20.7 mg/dl and 20.6 mg/dl, respectively. people in their twenties and those more than seventy had lower serum Lp (a) concentrations than people in any other age groups. However, there was no significant difference in serum Lp (a) concentration in their twenties and each of other age groups, or those more than seventy and each of other age groups.

3) Relationship between serum Lp (a) cocentration and the serum lipid levels, and liver function tests : According to serum Lp (a) concentration, two different groups were classified as follows : the high Lp (a) group, greater than or equal to 20 mg/dl ; the low Lp (a) group, less than 20 mg/dl (Table 2). No significant difference was noted in the average serum total cholesterol levels or triglyceride levels between these two groups. with respect to liver

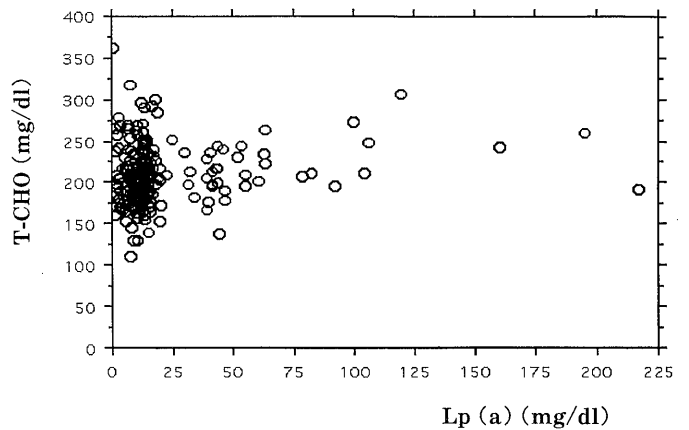


Fig. 2 Comparison between serum total cholesterol and Lp (a)

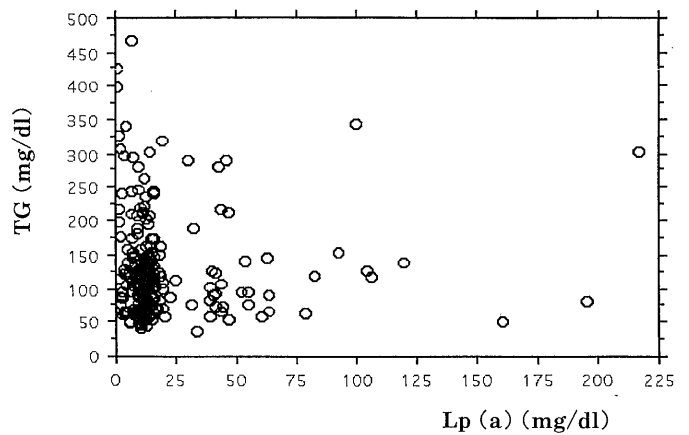


Fig. 3 Comparison between serum triglyceride and Lp (a) levels

function tests, the average values of GPT and r-GTP in the low Lp (a) group were significantly higher than those in the high Lp (a) group. However, other liver function tests such as GOT and Al-P showed no significant difference between the low Lp (a) and high Lp (a) groups. The relationship between serum lipid and Lp (a) levels is presented in Figures 2 and 3. Lp (a) concentration showed no correlation with serum total cholesterol or triglyceride levels.

Discussion

It has been reported that Lp (a), one of the glycoproteins, plays an important role in the development of atherosclerosis which causes ischemic heart and cerebral diseases, and that blood Lp (a) concentration is genetically regulated without any circumstantial influence^{4,5}.

The frequency distribution pattern of blood Lp (a) concentration of normal adults is known to differ by race. A similar frequency distribution pattern of Lp (a) was seen between Japanese and European people^{5,6}. Kawade et al. (7) also reported that 20 to 30% of Japanese people showed a low Lp (a) concentration with less than 10 mg/dl and the blood Lp (a) concentration of Japanese normal adults is assumed to form a shaped curve. Kawade et al. reported that the frequency distribution pattern of Lp (a) in Japanese people differed from that of Chinese, although both groups belong to the same Mongoloid race. The present study disclosed that Okinawan people showed an initial and largest peak in the frequency distribution of serum Lp (a) between 10 and 15 mg/dl, and a second peak between 40 and 45 mg/dl. Furthermore, the total average of Lp (a) concentration of northern Okinawan people was 20.7 mg/dl, which was obviously higher than that in any other report in Japan or China, but almost the same as that of India⁹. As indicated by other reports, we found no difference in Lp (a) concentrations by age or gender.

Although serum total cholesterol and triglycerides as well as Lp (a) are considered to be risk factors for atherosclerosis, levels of these substances showed no correlation in healthy subjects in this study. It has been also reported that various materials such as Lp (a), lipoprotein, and enzymes are produced in the liver, and that the Lp (a) concentration is reduced in liver diseases^{8,9}. However, the present study demonstrated higher level of serum GPT or r-GTP in the low Lp (a)

group. The concentration of Lp (a) showed no correlation with those of albumin or cholinesterase in healthy subjects. At the present time, it remains unclear whether serum Lp (a) is related to the development of atherosclerosis or shows different serum responses under normolipidemic and hyperlipidemic conditions.

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