

C3 POLYMORPHISM IN HYPERLIPOPROTEINEMIA (HLP)

D.D. Farhud, M.D., Ph.D., M.G.

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ABSTRACT

C3 typing was performed, by agarose gel electrophoresis, in 147 German patients suffering from hyperlipoproteinemia. The control group consisted of 322 healthy Germans. High frequencies of non-typeable sera, varying between 16.66 and 35.71% in different HLP types, found in the present investigation are notable and are a clue for chemical denaturation of C3 protein in HLP patients. Statistical analysis showed significant results ($P > 0.001$) in all five HLP types, as well as in the total, in comparison with the control group.

INTRODUCTION

In 1968, using a system of high-voltage agarose gel electrophoresis, genetically determined polymorphism of human C3, was demonstrated(1). Two codominant alleles at an autosomal locus on chromosome 19, determine three

Dept. of Human Genetics and Anthropology, School of Public Health, Tehran Univ. of Med. Sc., P.O. Box 14155-6446, Tehran-Iran.

C3 protein in hyperlipoproteinemic patients.

The determination of C3 types was performed according to the high-voltage agarose gel electrophoretic method (8).

RESULTS AND DISCUSSION

The distribution of C3 phenotypes and C3F gene in patients and the control group is shown in Table 1. As it can be seen from the Table, high frequencies of non-typeable sera, varying between 16.66 and 35.71% in different types of HLP, found in the present investigation, are notable.

High FF phenotype frequency (20%) in HLP type III (with high cholesterol and triglyceride) is in agreement with that found in atherosclerosis(12), also high frequency of the phenotype SF(45.28%) in type IV confirmed that of other investigation (6) in hyperlipidemic patients (44.89%). Statistical analysis (Table 1) showed significant results in all five HLP types as well as in the total ($P > 0.001$). The following points are remarkable:

1. The highest frequency of non-typeable sera (35.71%) in type V (high triglyceride, low cholesterol level) together with the lowest one (16.66%) in type II a (low triglyceride, high cholesterol level) seem to indicate that the frequency of non-typeable samples is related with triglyceride and not with cholesterol level in the serum.
2. High frequency of the SS phenotype (66.66%) together with low frequency of non-typeable sera (16.66%) in type

II a, and inversely low frequency of the phenotype SS (28.57%) together with high frequency of non-typeable sera (35.71%) in type V indicate that non-typeable samples are mostly from the SS phenotype.

3. In 19 out of the total of 34 non-typeable patients C3 typing was performed again in the period after the treatment and frequencies of the three C3 phenotypes were found to be SS (84.21%), SF (15.78%) and FF(0.00%).

4. Other investigations(6) showed that about 20% of HLP patients did not have any visible C3 bands, though 2 bands in front of the transferrin, not observed in normal, were seen (Fig 1). Therefore, the result of the present study confirms that of the previous study (6). This phenomenon was seen normally in older sera from healthy persons and sometimes in sera from diabetic and hepatitis patients.

In conclusion it is recommended that C3 typing and measurements should be done on a large sample size of HLP patients(prim.familial and secondary forms separately)to find an involvement or a causal inter-relationship of C3 in lipid synthesis.

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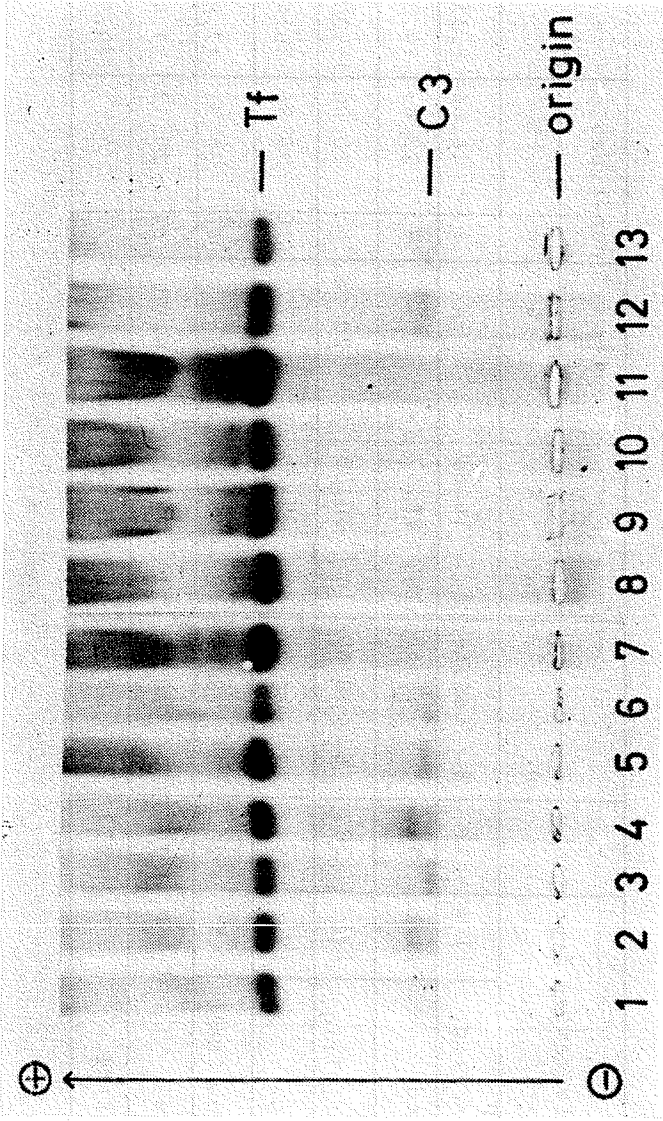


Fig. 1: Agarose gel electrophoresis of C3 phenotypes in normal and hyperlipidemic sera (Farhud et al 1972).

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Table 1: C3 Types in Hyperlipoproteinemia (HLP)

Hyperlipoproteinemia Type	N	SS		SF		FF		non-typable		F _{C3}	X ²	d. f. = 3	P
		n.	%	n.	%	n.	%	n.	%				
β -LP high chol.+low Trig.	12	8	66.66	2	16.66	-	-	2	16.66	8.33	55.00	p<0.0	
Mixed	35	17	48.57	10	28.57	-	-	8	22.85	14.28	76.07	p<0.0	
Abnorm. β -LP Chol.+Trig.	20	6	30.00	6	30.00	4	20.00	4	20.00	35.00	81.08	p<0.0	
Pre β -LP Trig.	53	17	32.07	24	45.28	2	3.77	10	18.86	26.41	70.61	p<0.0	
Pre β -LP high Trig.+low Chol.	28	8	28.57	10	35.71	-	-	10	35.71	17.85	121.21	p<0.0	
Total	147	56	38.09	51	34.69	6	4.08	34	23.13	21.42	92.79	p<0.0	
Control	322	206	63.97	106	32.92	10	3.10	-	-	19.56			

common phenotypes, SS, SF and FF. Several rare variants due to mutated alleles at the C3 locus have been described by different authors (2,7,11).

The different phenotypes of the C3 polymorphism seem to have different biological properties, as shown by their association with various diseases(5,6). A significant association with the C3 polymorphism has been found in atherosclerosis(12). and hypercholesterolemia (3,4).

In the present study the distribution of C3 phenotypes, together with frequencies of non-typeable sera, in different types of HLP is reported.

MATERIALS AND METHODS

C3 phenotypes were determined in 147 hyperlipoproteinemic patients and 322 healthy controls from Germany. The diagnosis of hyperlipoproteinemia types was performed in the Fat Lab. of the University Hospital, Mainz, FRG, using lipoprotein electrophoresis on agarose gel. The differentiation of HLP types was in accordance with the classification of Fredrickson (9,10).

In the present study separation of primary(familial) and secondary HLP types was not possible and age and sex of the patients were not considered either.

The milky appearance of non-typeable sera, due to high fat concentration, disappeared after extensive centrifugation, but electrophoresis of clear sera give no C3 bands, which is a clue for chemical denaturation of