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Occurrence of Antibodies to Human Coronavirus OC43 in Finland

HELLEVI RISKI and TIMO ESTOLA

From the Department of Virology, University of Helsinki, and State Veterinary Medical Institute, Helsinki, Finland

ABSTRACT. The occurrence of hemagglutination-inhibiting antibodies to human coronavirus OC43 was investigated in a material of random sera in Finland from 283 subjects including children and adults. Antibodies were found in 172 (60.8%). The highest incidence of positive sera was obtained from the age groups between 21 and 50 years—about 85% of the investigated sera were positive in these age groups. It can be concluded that infections with OC43 or related coronaviruses are rather common in Finland.

INTRODUCTION

Recently a new virus group, coronavirus, has been recognized as an important aetiological factor in mild respiratory diseases of the common cold type in man. Hartley et al. (6) were the first to indicate the occurrence of human infections caused by coronaviruses. They performed serological tests on military personnel at 3 posts in different parts of the USA. The specimens were taken in connection with respiratory epidemics in the winter months. Examination of paired sera revealed that 21.8% of the patients had developed a 4-fold or greater rise in complement-fixing antibody titer to mouse hepatitis virus (MHV). MHV is a member of the corona group and has antigens which cross react with human coronaviruses. The first isolations of human coronaviruses were reported in 1965 in England (10) and in 1966 in the USA (5), and the isolates were obtained from typical common cold cases.

About 20 strains have been isolated so far. They can be divided into at least 3 serologic groups of closely related strains. There is evidence of some cross reactions and heterologous responses between these groups (1).

Recent seroepidemiologic studies of coronavirus infections in man have revealed that antibodies to human coronavirus strains are common in the USA (4), England (3), Japan (9) and the USSR (11). The present report describes the occurrence of antibodies to one human coronavirus strain OC43 in sera sent to the Department of Virology, Helsinki University, for various diagnostic purposes.

MATERIAL AND METHODS

Sera

The material consisted of 283 randomly selected diagnostic serum samples from patients suffering from an acute disease with suspected viral aetiology. The samples were sent from different parts of the country, mainly from southern Finland. They were first inactivated at 56°C for 30 min and then stored at -20°C until used. Some positively reacting sera were re-investigated after kaolin or KJO₄ treatment. In the tests, the sera were screened using 2-fold dilutions in saline from 1:8.

Antigen

The antigen used was a brain suspension of suckling mice containing OC43 virus. This was produced by inoculating 0.02 ml of diluted OC43 virus suspension intracerebrally into 3-day old suckling mice. The inoculated mice showing typical encephalitic symptoms, usually within 72–90 hours, were sacrificed and the brains were harvested. A 10% suspension of brain was made in Difco nutrient broth. The brain suspension was clarified by centrifugation. The antigen was stored at -70°C.

Hemagglutination (HA) titration

Titration of hemagglutinating activity of OC43 virus was performed by the microtiter technique using 2-fold dilutions of antigen suspensions and equal quantities of 0.5% suspension of chicken erythrocytes. The result of the HA test was read after 30 min at 20°C. The end point of HA was estimated visually and was considered to be the highest dilution in which a positive pattern was present. The end point dilution corresponds to one HA unit.

Hemagglutination inhibition (HI) test

2-fold dilutions in saline were prepared of the sera to be tested, starting with a dilution of 1:8. Equal amounts of serum dilution and antigen dilution containing 4 HA units were mixed. After 10 min at 20°C the same amount of 0.5%

Table I. Occurrence of HI antibodies to coronavirus OC43 (titer ≥ 8) among 283 random sera

Age group (years)	No. positive sera/ no. tested	No. positive sera with a titer of					% positive sera
		8	16	32	64	128	
0- $\frac{1}{2}$	6/16	2	4	0	0	0	37
$\frac{1}{2}$ -5	18/44	8	9	1	0	0	42
6-10	8/23	2	5	0	1	0	35
11-20	22/38	6	9	6	1	0	58
21-30	34/40	4	16	10	3	1	85
31-40	18/21	4	7	5	1	1	86
41-50	28/33	4	15	8	0	1	85
51-60	13/24	1	8	1	2	1	54
61-70	14/24	6	4	3	1	0	58
>70	11/20	2	6	3	0	0	55
Total	172/283	39	83	37	9	4	60.8

chicken erythrocytes was added and the mixtures were incubated for 30 min at 20°C. The highest serum dilution causing complete inhibition of hemagglutination was taken as the antibody titer. Serum, antigen, positive serum and erythrocyte controls were included in every HI test.

RESULTS

The occurrence of HI antibodies to OC43 virus in different age groups is shown in Table I. Out of the total material of 283 random sera, 172 (60.8%) had HI antibodies (titer ≥ 8). The highest incidence of positive sera and also most of the highest titers were detected in the age range 21 to 50 years. The percentage of positive serum samples was about 85% in these age groups. Because of the possible role of maternal antibodies, the first age group of the table was limited to between newborn and 6-month old children.

The titer values varied from 8 to 128. The most common titer was 16 which was obtained in about 48% of the positive sera. Neither kaolin nor potassium periodate treatment had any effect on the titers of the positive sera.

DISCUSSION

It can be concluded from the present results that infections with human coronavirus OC43 or closely related coronaviruses are rather common in Finland. Most of the population of middle age has been exposed to this type of virus.

The titers observed here were in most cases fairly low and typical of response to the infective organism long before the sampling.

This is the first report concerning the occurrence of human coronaviruses in the Scandinavian

countries. The results agree well with those obtained in England, the USA and the USSR (3, 7, 8, 11). The correlation between the occurrence of OC43 antibodies and clinical diseases in Finnish populations is still undetermined.

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Address for reprints:

*T. Estola, V.M.D.,
State Veterinary Medical Institute,
Hämeentie 57,
SF-00550 Helsinki 55,
Finland*