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The Analysis of Yellow Fever Virus Antibody in Human Serum from Epidemic Areas of Tianjin Port, 2013

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Abstract

Objective: To investigate the prevalence and distribution characteristics of yellow fever virus antibody in human serum from epidemic areas of Tianjin port in 2013 and assess the situation of yellow fever virus in different countries in order to provide evidence for the prevention and control of yellow fever virus.

Methods: The people from epidemic areas were selected as study object. 260 samples were collected together with detailed personal information. Each sample contained 5 ml venous blood. ELISA was used to detect the yellow fever virus antibody. The dengue virus antibody and west Nile virus antibody were detected in positive samples. Statistical analysis was used to compare differences of the positive rates between different nationalities, gender, occupation, age, and entry time.

Results: All respondents came from Africa and South America, the total positive rate of serum antibody to yellow fever virus was 25.38%. Of which, the positive rate of South American personnel was relatively high, up to 27.27%. There was no significant difference in positive rate between different genders. The >40 year old age group was the highest, up to 42%. The positive rate of labor workers was relatively high, up to 45.24%. In the time distribution, the positive rate of fourth-quarter entry personnel was relatively high, up to 31%.

Conclusion: The yellow fever vaccination rate of people from epidemic areas in 2013 was low. These people pose a threat to public health security of china as a potential source of infection. There was a significant difference in the detection rate of yellow fever virus antibody among people with different ages and occupations

Keywords

Tianjin port; Yellow fever virus; Antibody detection

Introduction

Yellow Fever (YF) is an acute infectious disease caused by Yellow Fever Virus (YFV), which is one of the three infectious diseases of international health regulations [1]. YFV belongs to flavivirus, transmitted through the medium of mosquito among vertebrates [2]. The main clinical symptoms are fever, jaundice, hemorrhage and proteinuria, 5% to 20% of patients manifested clinical symptoms, a small number of patients came to severe case and death [3]. According to WHO, there are at least 200 thousand cases of YF in the world each year, and 30 thousand people lose their lives [4]. Since December 2016, Brazil has been affected by an unusually large and expanding yellow fever (YF) outbreak, with over 3500 suspected cases reported and several hundred deaths [5]. Because no special treatment for yellow fever was used, YFV 17D vaccine injection is the most effective means of prevention of YF currently [6].

YF is endemic in tropical regions of Africa and South America, but there may be cases of imported cases all over the world with the acceleration of global integration [7]. As a large commercial city in the North of China, Tianjin is an important channel for trade between North China and the world. In our study, YFV antibody screening was conducted to personnel from Africa and South America of Tianjin port in 2013. To analysis the popular features through observing the situation of people carrying YFV related antibody. According to the difference of antibody positive rate among different regions, genders, ages, occupations and time, differentiate the key population to provide a basis for the prevention and detection of YF.

Objects and Methods

Objects

Identify people of Tianjin port from Africa and South America as survey object, January 1, 2013 to December 31, 2013. 5 ml venous blood was collected and serum was gain

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through low speed centrifugation. Then the YFV antibody detection was conducted.

Methods

YFV antibody test: All samples were detected by Human Yellow fever virus antibody ELISA Kit (made by QIYI Shanghai Technology Co., Ltd.), which was used to detect the level of serum antibody by indirect ELISA. Recombinant envelope protein of YFV was used as antigen for coating plates. The experiment included negative control, positive control and blank control. To each well 100 μl of a sample was added except for control wells, and then incubated at 37° C for 30 minutes. After washing five times, each well was added 100 μl HRP labeled sheep anti human IgG, then the plate was incubated at 37° C for 30 minutes. After washing five times, a chromogenic agent A and B solution were added to each well to develop the color and the plate was read at 450 nm for Optical Density (OD). A serum sample was considered to contain SFTSV specific antibody when absorbance of the sample ≥ threshold value (cutoff). The threshold value = 0.10 + the average OD value of the negative control (if the OD value of a negative control was less than 0.04, it was considered as 0.04).

West Nile virus antibody test: The west Nile virus antibody was detected in positive samples to reduce cross reactivity. Human west Nile virus antibody ELISA Kit (made by QIYI Shanghai Technology Co., Ltd.) was used to detect west Nile virus antibody by indirect ELISA. The operation steps are shown as 4.2.1.

Dengue virus antibody test: The dengue virus antibody was also detected in positive samples to reduce cross reactivity. And indirect ELISA method was utilized to detect dengue virus antibody. The antigen used in indirect ELISA was Dengue virus type1-4 E protein domain III fusion protein expressed in eukaryotic system (made by our department). Other operating steps as described above.

Quality control: Blood sampling and processing sites, operating process and preservation condition were strictly qualified. Standard blood collection tools were provided to guarantee the sampling. We repeated all the samples detection twice to verify the result, and repetition will stop only if the result of the two inspections is identical with each other.

Informed consent: The study was approved by the Ethic Committee of Tianjin exit inspection and Quarantine Bureau. Blood samples were collected at International Travel health care center and all operations were strictly compliance with the provisions of the state on the entry of personnel management. Immigrants knew and agreed to collect serum, then had a physical examination.

Statistical analysis: Parallel the questionnaire using Epidata 3.2 software. After verification, import it into SAS 9.2 statistical software to make a statistical analysis.

Results

Basic situation

A total of 260 serum samples were collected from 34 countries of two continents. Of which, 150 samples were from 28 countries of Africa and 110 samples were from 6 countries of South America. In 34 countries, detection of YFV antibody in sera from 19 countries was positive, with total of 215 cases, and the positive rate 30.70%. And detection of YFV antibody in sera from 15 countries was negative, with total of 45 cases. As shown in Table 1.

The area distribution of YFV antibody detection

The YFV antibody detection rate in African was 24%, while that in South American was 27.27%. The YFV antibody detection rate of South American was higher than that of African, but the difference was not statistically significant (χ^2=0.359, P=0.549). In addition, The YFV antibody was detected in people from 16 African counties out of 28, with 57.14% positive rate, and 3 South American countries out of 6, with 50% positive rate. No significant difference was found in the detection rate of national distribution (χ^2=0, P=1). As shown in Table 1 and 2.

The gender distribution of YFV antibody detection

YFV antibody detection rate in male was 24.75%, while that in female was 27.59% among entry-personnel. However, there was no significant difference in detection rate (χ^2=0.191, P=0.662), for details see attached Table 2.

The age distribution of YFV antibody detection

All respondents were divided into four groups, <20 age group, 20-30 age group,30-40 age group and >40 age group. It was found that the positive rate of >40 age group was highest, up to 42%, the positive

Country	Number	Positive number	Positive rate	Country	Number	Positive number	Positive rate
Egypt	16	1	6.25%	Algeria	2	0	0
Ethiopia	4	1	25%	Guinea	2	0	0
Benin	2	1	50%	Burundi	2	0	0
Somalia	2	1	50%	Eritrea	1	0	0
Congo	6	1	16.67%	Djibouti	3	0	0
Angola	5	4	80%	Zimbabwe	3	0	0
Kenya	10	3	30%	Ghana	1	0	0
Madagascar	3	1	33.33%	Gabon	1	0	0
Mauritius	3	1	33.33%	Mali	1	0	0
Morocco	8	1	12.5%	South Africa	4	0	0
Sierra Leone	12	4	33.33%	Nigeria	8	0	0
Cameroon	4	2	50%	Sultan	6	0	0
Tanzania	19	8	42.11%	Peru	1	0	0
Tunisia	1	1	100%	Venezuela	5	0	0
Uganda	11	3	27.27%	Chile	5	0	0
Zambia	10	3	30%				
Argentina	24	2	8.33%				
Brazil	52	20	38.46%				
Columbia	23	8	34.78%				
Total	215	66	30.70%		45	0	0

Table 1: The national distribution of yellow fever virus antibody detection.

Feature	Number	Constituent ratio	Positive number	Positive rate
Area				
Africa	150	57.69%	36	24.00%
South America	110	42.31%	30	27.27%
x^2 value				0.359
p value				0.549
National distribution				
Africa	28	82.35%	16	57.14%
South America	6	17.65%	3	50.00%
x^2 value				0.
p value				1
Sex				
male	202	77.69%	50	24.75%
female	58	22.31%	16	27.59%
x^2 value				0.191
p value				0.662
Age				
<20	25	9.61%	9	36%
20-30	86	33.08%	22	26%
30-40	99	38.08%	14	14%
>40	50	19.23%	21	42%
x^2 value				15.384
p value				0.002
Occupation				
labor workers	42	16.15%	19	45.24%
students	162	62.31%	35	21.60%
Technical personnel	56	21.54%	12	21.43%
x^2 value				10.425
p value				0.005
Time				
First and second quarter	56	21.54%	3	18%
Third quarter	72	27.69%	6	21%
Fourth quarter	132	50.77%	21	31%
x^2 value				4.708
p value				0.095
Total	260		66	25.38%

Table 2: The comparison of yellow fever virus antibody test results with different characteristics

rate of 30-40 age group was lowest, up to 14% through comparing differences of YFV antibody detection rate among groups. And there was significant difference in detection rate (χ^2=15.384, P=0.002), for details see attached Table 2.

The occupation distribution of YFV antibody detection

The survey involved 3 occupations, labor workers, students and technical personnel. It was found that the positive rate of labor workers was highest, up to 45.24%, the positive rate of technical personnel was lowest with 21.43%. Through comparing differences of YFV antibody detection rate among groups, we found that the detection rates were statistically significant different (χ^2=10.425, P=0.005), for details see attached Table 2.

The time distribution of YFV antibody detection

According to entry time, the samples were divided into four groups, the first quarter, the second quarter, the third quarter and the fourth quarter. As statistical results shown, the positive rate of the fourth quarter was highest, up to 31%, and there was no significant difference in the detection rate among other groups, for details see attached Table 2.

Discussion

At present, several kinds of YFV detection technology were applied to practical work: (1) virus isolation, such as C6 / 36 (or BHK21) cells; (2) detection of virus nucleic acid by RT-PCR; (3) detection of virus antigen, virus antigen can be directly detected by antigen capture ELISA and immunoenzymatic assay; (4) Serological detection, including HI, CF, Neutralizing Antibody (NT), and IgM, IgG antibodies (EIA). Of which, virus isolation and nucleic acid detection does not apply to the actual work of the port because the methods were complicated and required high requirement for the conditions of laboratory [8,9]. In our study, we utilize Elisa method to detect YFV antibody in different groups and analysis epidemic characteristics, in order to strengthen the monitoring and control of YFV in port.

There are three mainly possibilities when the detection of YFV antibody is positive. 1) People were infected with YFV recently. 2) People were injected with vaccine 3) People were infected with other similar flavivirus recently. According to the WHO regulations, YFV 17D vaccine is a vaccine that is required for vaccination among member countries. It belongs to the mandatory vaccination for international travel [10]. In 2013, 5 immigrants without yellow fever vaccination certificate were found in Shenzhen port and the YF antibody detection of sera were all negative [11].

In this study, only 2 people had a clear history of vaccination. 4 of them had overseas vaccination certificates, but there were no effective labels for vaccine manufacturers and batch numbers, and it

was hard to recognize its effectiveness. Hence, it is necessary to test the YFV antibody of passengers of Tianjin port. Results show that 3 out of 6 people had YFV antibody, indicating that vaccination can effectively produce antibodies, but the proportion of vaccination is low.

It was reported that YFV and other arboviruses share partial antibody such as Dengue virus, West Nile virus [12, 13]. In order to eliminate the influence of cross antibody, the YFV antibody-positive samples were detected for dengue virus and west Nile virus antibody, respectively. Based on the experimental results, 2 cases out of 66 were positive for dengue virus antibody and none was positive for Nile virus antibody. Because it has little effect on the results of epidemiological investigation, it is not included in consideration. Therefore, our data shows that the samples may be infected with YFV in the near past years, and it also can reflect the prevalence of local population.

In our study, the positive rates of Africa and South America were 24% and 27.27%, respectively. There was no statistical difference demonstrating that the two continents had different degrees of yellow fever virus natural infection, but the severity difference could not be distinguished. In the respect of country distribution, no statistical difference was found between people from nearly African countries and South American countries. There was no statistical difference between male and female indicating that gender was not the influence factors of YFV infection, and this was also consistent with the epidemiological characteristics of other arbovirus infections. In terms of age distribution, the positive rate of >40 years group was the highest, 30-40 years old group was the lowest, and the difference was statistically significant. It showed that age was the influence factors of YFV infection. This was consistent with the characteristics of infection of other arboviruses. In general, the longer exposure in the viral cycle, the greater chance of being infected. Three occupations were involved in our survey, of which the positive rate of labor workers was the highest, and there was significant difference between different occupations. Occupation is also an important factor in other arbovirus natural infection. People who are engaged in field work and outdoor physical work are more likely to be bitten by mosquitoes and be infected with YFV. This characteristic was similar with other arbovirus infections. In general, arbovirus infections were closely related to season and temperature. With the breeding of mosquitoes in the summer, the incidence of arbovirus infection increased significantly, but this feature is not obvious in tropical areas with little change in temperature. In our study, the positive rate of the fourth quarter was the highest but there was no statistical difference compared with the other quarters. It showed that the entry time was not the influencing factors.

In summary, our investigation reveals that YFV infection is endemic in Africa and South America and the virus is also widely distributed in two continents. Therefore, the port quarantine officers need to take effective prevention and control measures to those who come from epidemic area, such as increasing the intensity of vaccination certificate inspection. At present, there are some loopholes in the inspection of YFV vaccination certificate, and it is difficult to achieve the 100% inspection of people from the epidemic areas. According to the results of our study, occupation is the influence factors of detection of YFV antibody, which suggests that we should focus on the key population when conducting quarantine. Enhance the purpose of quarantine inspection, to achieve early detection, early diagnosis and early treatment and reduce the risk of yellow fever transmission [14].

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