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Yellow Fever Virus Antibody in Human Serum of Epidemic Areas, Tianjin，China, 2014

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ABSTRACT

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. We tested people from epidemic areas of Tianjin port in 2014 to investigate the prevalence and distribution characteristics of yellow fever virus antibody. 192 samples were collected and the positive rate of yellow fever virus antibody was 22.92%. The positive rates among different countries, genders, ages, occupations and entry time were calculated and analyzed. There were significant difference in the detection rate of YFV antibody among people with different age groups and occupations. The positive rate of people >40 age and workers engaged in labor were relatively high and had statistical significance compared to other groups.

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Abbreviation: YF,Yellow Fever; YFV, Yellow Fever Virus

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Introduction

Yellow fever (YF) is an acute infectious disease, endemic to tropical regions. YF principally affects humans and nonhuman primates, and the main clinical symptoms are fever, jaundice, hemorrhage and proteinuria[1]. Yellow fever virus (YFV) was the agent of YF, which belongs to flavivirus and transmitted through the medium of mosquito among vertebrates [2]. According to WHO, there are at least 200 thousand cases of YF in the world each year, and 30 thousand people lose their lives[3]. Since December 2016, Brazil has been affected by an unusually large and expanding YF outbreak, with over 3500 suspected cases reported and several hundred deaths [4]. So far, no special treatment for yellow fever was utilized and YFV 17D vaccine injection was the most effective means of prevention of YF [5]. 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 [6]. And YF is a continued threat to people who travel to these regions without vaccination [7]. As a large commercial city in the North of China, Tianjin is an important channel for trade between North China and the world. Here we conducted YFV antibody screening to personnel from Africa and South America of Tianjin port in 2014 and analysis the difference of antibody positive rates among regions, genders, ages, occupations and entry-time, in order to provide a basis for the prevention and detection of YF.

Materials and Method

During January 1 to December 31, 2014, we collected blood samples from people of Tianjin port, who came from Africa and South America. Blood samples were collected at Tianjin International Travel health care center and all operations were strictly compliance with the provisions of the state on the entry of personnel management. Donors agreed to collect serum and signed a written agreement. 5ml venous blood was collected and serum was gain through low speed centrifugation. The study was approved by the Ethic Committee of Tianjin exit inspection and Quarantine Bureau.

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. The dengue virus antibody and west nile virus antibody were also detected in positive samples to reduced cross reactivity. Human west nile virus antibody ELISA Kit (made by QIYI Shanghai Technology Co., Ltd.) was used to detect west nile virus antibody. 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 Lab).

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

Results and Conclusion

A total of 192 serum samples were collected from 30 countries of two continents. Of which, 130 samples were from 25 countries of Africa and 62 samples were from 5 countries of South America. In 30 countries, detection of YFV antibody in sera from 21 countries was positive, with total of 160 cases, and the positive rate 27.50% (44/160). And detection of YFV antibody in sera from 9 countries was negative, with total of 32 cases.

The YFV antibody detection rate in African was 20%, while that in South American was 29.03%, but the difference was not statistically significant(χ^2=1.939， P=0.164). It demonstrated that the two continents had different degrees of yellow fever virus natural infection, but the severity difference could not be distinguished. In addition, The YFV antibody was detected in people from 17 African counties out of 25, with 68% positive rate, and 4 South American countries out of 5, with 80% positive rate. No significant difference was found in the detection rate of national distribution(χ^2=0, P=1). As shown in Table 1.

YFV antibody detection rate in male was 24.16%, while that in female was 18.60% among entry-personnel. However, there was no significant difference in detection rate (χ^2=0.583, P=0.445). This was also consistent with the epidemiological characteristics of other arbovirus infections, for details see attached Table 1.

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 34.38%, the positive rate of 30-40 age group was lowest, up to 13.64% through comparing differences of YFV antibody detection rate among groups. And there was significant difference in detection rate(χ^2=11.624, P=0.009). 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.

The survey involved 3 categories of occupations, labor workers, students and technical personnel. It was found that the positive rate of labor workers was highest, up to 30.61%, the positive rate of technical personnel was lowest with 16%. Through comparing differences of YFV antibody

Table1. The comparison of YFV antibody test results with different characteristics

Feature	Number	Constituent ratio	Positive number	Positive rate
Area				
Africa	130	67.71%	26	20.00%
South America	62	32.29%	18	29.03%
x^2 value				1.939
p value				0.164
National distribution				
Africa	25	83.33%	17	68.00%
South America	5	16.67%	4	80.00%
x^2 value				0.
p value				1
Sex				
male	149	77.60%	36	24.16%
female	43	22.40%	8	18.60%
x^2 value				0.583
p value				0.445
Age				
<20	22	11.46%	3	13.64%
20-30	51	26.56%	8	15.69%
30-40	55	28.65%	9	16.36%
>40	64	33.33%	24	37.50%
x^2 value				11.624
p value				0.009
Occupation				
labor workers	98	51.04%	30	30.61%
students	44	22.92%	6	13.64%
Technical personnel	50	26.04%	8	16.00%
x^2 value				6.785
p value				0.034
Time				
First and second quarter	42	21.87%	10	23.81%
Third quarter	56	29.17%	14	25%
Fourth quarter	94	48.96%	20	21.28%
x^2 value				0.3
p value				0.861
Total	**192**		**44**	**22.92%**

detection rate among groups, we found that the detection rates were statistically significant different(χ^2=6.785，P=0.034), for details see attached Table 1. 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 [8, 9].

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 third quarter was highest, up to 25%, and there was no significant difference in the detection rate among other groups. (χ^2=0.3， P=0.861). It showed that the entry time was not the influencing factors in this investigation. 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.

There are three mainly possibilities when the detection of YFV antibody in sera is positive: (1) Past exposure to YFV; (2) Injection with relevant vaccine and (3) Past exposure to other similar flavivirus. It was reported that YFV and other arboviruses share partial antibody such as Dengue virus, West Nile virus [10, 11]. 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. Results showed that 2 cases out of 44 were positive for dengue virus antibody and none was positive for west Nile virus antibody. Although we can't distinguish them in this study, it has little effect on the results of epidemiological investigation. In addition, only 2 people had a clear history of vaccination and 4 people had overseas vaccination certificates, but there were no effective labels for vaccine manufacturers and batch numbers, and it was hard to recognize its effectiveness. Therefore, we argue that the result can reflect the prevalence of local population and most of the positive samples were infected with YFV in the near past years.

In summary, we reveal that YFV infection is endemic in Africa and South America and the virus is also widely distributed in two continents currently. 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 our results, age and occupation are the influence factors of detection of YFV antibody, which

suggests that we should focus on this population when conducting quarantine. Limitations of our study are obvious. Firstly, the subjects were brought into the survey passively rather than sampling actively. Hence, the results may not reflect all epidemiological features accurately. Secondly, the size of sample is too small. Data of several years are needed to obtain more accurate results. Thirdly, other important cross antibodies were not excluded, such as the Zika virus. False positive samples may exist in our study.

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