Research Article

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

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Abstract

Objective: *To investigate the prevalence and distribution characteristics ofyellow fever virus(YFV) antigen in human serum from epidemic areas in 2013.*

Methods: *The people from the yellow fever epidemic areas of Tianjin port were selected as study object.260 samples were collected together with detailed personal information. And each sample contained 5ml venous blood. Indirect ELISA was used to detect YFV antigen. The dengue virus antigen and west nile virus antigen were also detected in positive samples to reduced cross reactivity. Positive rate was calculated. Statistical methods were used to compare the differences of the positive rates between different countries, genders, ages, occupations and entry time.*

Results: *All respondents came from Africa and South America. The total positive rate of serum antigenofYFV was 11.54%(30/260). Of which, the positive rates of African and South American people were 12% and 10.91%, respectively. The positive rates of male and female were 11.88% and 10.34%, respectively. The positive rate of >40 year old age group was the highest, up to 14%. In the time distribution, the positive rate of fourth-quarter entry personnel was up to 15.91%.There was no significant difference in positive rate between different countries, genders, ages, and entry time, except occupations. Workers engaged in labor service positive rate was 35.71%.*

Conclusion: *TheYFVantigen positive rate of people from epidemic areas in 2013 was high. These people carrying pathogens 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 YFV antigen among people with different occupations.*

Keywords: Tianjin port; Yellow fever virus; Antigen detection
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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 antigen screening was conducted to personnel from Africa and South America of Tianjin port in 2013.To analysis the popular featuresthrough observing the situation of people carrying YFV related antigen. According to the difference of antigen positive rate among different regions, genders, ages, occupations and time, differentiate the key population to provide a basis for the prevention and detection ofYF.

Objects and Methods

Objects

Identify people of Tianjin port from Africa and South America as survey object, January 1, 2013 to December 31, 2013.5ml venous blood was collected and serum was gain through low speed centrifugation. Then the YFV antigen detection was conducted.

Methods

All samples were detected by Human Yellow fever virus antigen

ELISA Kit (made by QIYI Shanghai Technology Co., Ltd.), which was used to detect the level of serum antigen by indirect ELISA. The dengue virus antigen and west nile virus antigen were also detected in positive samples to reduced cross reactivity. Human west nile virus antigen ELISA Kit (made by QIYI Shanghai Technology Co., Ltd.) was used to detect west nile virus antigen. Andindirect ELISA method was utilized to detect dengue virus antigen. The antibody used in indirect ELISA was anti-dengue virus type1-4 E protein domain III fusion protein sera produced in rabbit (made byour department).

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

1. 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 antigen in sera from 15 countries waspositive, with total of 176 cases, and the positive rate 17.05%. And detection of YFV antigen in sera from 19 countries was negative, with total of 84 cases. As shown in Table 1.

Table1: The national distribution of yellow fever virus antigen detection

Country	Number	Positive Number	Positive Rate	Country	Number	Positive Number	Positive Rate
Egypt	16	2	12.50%	Madagascar	1	0	0
Ethiopia	8	1	25.00%	Djibouti	2	0	0
Benin	2	1	50.00%	Guinea	2	0	0
Somalia	1	1	50.00%	Burundi	2	0	0
Congo	8	1	33.33%	Eritrea	2	0	0
Kenya	4	1	10.00%	Ghana	2	0	0
Mauritius	1	1	33.33%	Gabon	1	0	0
Sierra leone	5	1	8.33%	Zimbabwe	4	0	0
Angola	3	1	20.00%	Cameroon	1	0	0
Tanzania	21	1	11.11%	Morocco	1	0	0
Tunisia	2	1	100.00%	Mali	1	0	0
Uganda	11	2	18.18%	South Africa	5	0	0
Zambia	18	1	20.00%	Nigeria	11	0	0
Brazil	12	4	15.38%	Sultan	8	0	0
Columbia	3	1	17.39%	Algeria	1	0	0
				Peru	1	0	0
				Venezuela	3	0	0
				Chile	2	0	0
				Argentina	4	0	0
Total	176	30	17.05%		84	0	0

2. The area distribution of YFV antigen detection The YFV antigen detection rate in African was 12%, while that in South American was 10.91%. The YFV antigen detection rate of African was higher than that of South American, but the difference was not statistically significant (χ^2=0.074, P=0.786). In addition, The YFV antigen was detected in people from 13 African counties out of 28, with 46.43% positive rate, and 2 South American countries out of 6, with 33.33% positive rate. No significant difference was found in the detection rate of national distribution (χ^2=0.018, P=0.894). As shown in Table 1 and 2.

3. The gender distribution of YFV antigen detection YFV antigen detection rate in male was 11.88%, while that in female was 10.34% among entry-personnel. However, there was no significant difference in detection rate (χ^2=0.104, P=0.747), for details see attached Tables 2.

4. The age distribution of YFV antigen 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 14%, the positive rate of 20-30 age group was lowest, up to 8.14% through comparing differences of YFV antigen detection rate among groups. And there was no

significant difference in detection rate (χ^2=1.594, P=0.69), for details see attached Tables 2.

5. **The occupation distribution of YFV antigen detection** The survey involved 3 categories of occupations, labor, students and technical personnel. It was found that the positive rate of labor was highest, up to 35.71%, the positive rate of students was lowest with 3.7%. Through comparing differences of YFV antigen detection rate among groups, we found that the detection rates were statistically significant different (χ^2=30.518, P=0.001), for details see attached Tables 2.

6. **The time distribution of YFV antigen 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 15.91%, and there was no significant difference in the detection rate among other groups, for details see attached Tables 2.

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

Feature	Numbers	Constituent Ratio	Positive Number	Positive rate
Area				
Africa	150	57.69%	18	12.00%
South America	110	42.31%	12	10.91%
x2 value				0.074
p value				0.786
National distribution				
Africa	28	82.35%	13	46.43%
South America	6	17.65%	2	33.33%
x2 value				0.018
p value				0.894
Sex				
male	202	77.69%	24	11.88%
female	58	22.31%	6	10.34%
x2 value				0.104
p value				0.747
Age				
<20	25	9.61%	3	12.00%
20-30	86	33.08%	7	8.14%
30-40	99	38.08%	13	13.13%
>40	50	19.23%	7	14.00%
x2 value				1.594
p value				0.69
Occupation				
contract workers	42	16.15%	15	35.71%
students	162	62.31%	6	3.70%
Technical personnel	56	21.54%	9	16.07%
x2 value				30.518
p value				0.001
Time				
First and second quarter	56	21.54%	3	5.36%
Third quarter	72	27.69%	6	8.33%
Fourth quarter	132	50.77%	21	15.91%
x2 value				5.291
p value				0.071
Total	260		30	11.54%

Discussion

At present, YF mainly exists in the form of endemic diseases in Africa and South America.However, the risk of cross-border spread of the epidemic cannot be ignored [8]. Between 1996 and 1999, four fatal cases occurredinunvaccinated travellers from the USA and Europe to Brazil (two cases), Venezuela, and Côte d'Ivoire[9]. In 1998, a small number of cases of urban yellow fever in the Americas was reported in Santa Cruz, Bolivia 35 —the first such episode since 1954[10]. In 2016, Beijing entry exit inspection and quarantine department confirmed the first case of imported YF cases on March 12, another 4 cases were found later. All five cases were returnees from Angola[11].Therefore, monitoring YF at the port is the key link in the whole epidemic prevention and control.

There are two mainly possibilities when the detection of YFV is positive. 1) People were infected with YFV recently. 2) People were infected with other similar flavivirus recently. It was reported that YFV and other arboviruses share partial antigen such as Dengue virus, West Nile virus [12,13].In order to eliminate the influence of cross antigen, the YFV antigen-positive samples were detected for dengue virus and west Nile virus antigen, respectively. Based on the experimental results, 2 cases out of 30 were positive for dengue virus antigen. Because it has little effect on the results of epidemiological investigation, it is not included.Therefore, the result shows that the samples may be infected with YFVin the near past years, and it also can reflect the prevalence of local population. Since 2009, the Guangdong inspection and Quarantine Bureau has been monitoring the entry personnel of Guangdong border port through detecting antigen[14]. In 2013,5 immigrants without yellow fever vaccination certificate were found and the YF antigen detection of sera were all negative[15].

In our study, based on the result of area distribution of YFV antigen detection, the positive rates of Africa and South America were 12% and 10.91%, respectively, between which there was no statistical difference. It demonstrated 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, people from nearly 47% of African countries and 33% South American countries were detected positive. And no statistical difference was found. The YFV antigen detection rates of male and female were 11.88% and 10.34%, respectively. There was no statistical difference 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, 20-30 years old group was the lowest, but the difference was not statistically significant. It showed that age was not the influence factors of YFV infection.This was not consistent with the characteristics of infection of other arboviruses, and may be related to the sample bias.In general,the longer exposure in theviral cycle, the greater chance of being infected.

Through collecting personal information our survey involved three occupations, of which the positive rate of contract 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 this investigation.

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 antigen, 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 [16].

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,there are large differences in the composition of immigration personnel in each port. Therefore, the result of Tianjin port cannot be extrapolated to other ports.

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