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The Analysis of Yellow Fever Virus Antigen in Human Serum from Epidemic Areas of Tianjin Port, 2012

Qi Jun[1], Li Guolei[2], Liu Yumei[2] and Niu Guoyu[2*]

[1]*Tianjin International Travel Health Care Center, Tianjin, 300456, P.R. China*

[2]*School of Public Health, WeiFang Medical University, 261053, China*

*Corresponding author: Niu Guoyu, School of Public Health, WeiFang Medical University, 261053, China, E-mail: niugy@wfmc.edu.cn

Abstract

Objective: To investigate the prevalence and distribution characteristics of yellow fever virus (YFV) antigen in human serum from epidemic areas of Tianjin port in 2012.

Methods: The people from the yellow fever epidemic areas of Tianjin port were selected as study object. 172 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 antigen of YFV was 11.63% (20/172). Of which, the positive rates of African and South American people were 10.96% and 15.38%, respectively. The positive rates of male and female were 11.68% and 11.43%, respectively. The positive rate of >40 year old age group was the highest, up to 17.24%. In the time distribution, the positive rate of third-quarter entry personnel was up to 14.94%.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 29.41%.

Conclusion: The YFV antigen positive rate of people from epidemic areas in 2012 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

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. Yellow fever poses a serious threat to human health [4]. Due to the lack of treatment effects of YF, YFV 17D vaccine injection is the most effective means of prevention of YF currently [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]. 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 2012. To analysis the popular features through 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 of YF.

Objects and Methods

1. Objects: Identify people of Tianjin port from Africa and South America as survey object, January 1, 2012 to December 31, 2012. 5 ml venous blood was collected and serum was gain through low speed centrifugation. Then the YFV antigen detection was conducted.

2. 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 antibody 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. And indirect ELISA method was utilized to detect dengue virus antigen. 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).

3. 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.

4. 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

5. 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 172 serum samples were collected from 38 countries of two continents. Of which, 146 samples were from 31 countries of Africa and 26 samples were from 7 countries of South America. In 38 countries, detection of YFV antigen in sera from 15 countries was positive, with total of 105 cases, and the positive rate 19.05%. And detection of YFV antigen in sera from 23 countries was negative, with total of 67 cases. As shown in Table 1.

Country	Number	Positive number	Positive rate	Country	Number	Positive number	Positive rate
Egypt	6	2	33.33%	Garner Nigeria	1	0	0
Ethiopia	8	1	12.50%	Djibouti	2	0	0
Benin	2	1	50.00%	Guinea	2	0	0
Somalia	1	1	100.00%	Burundi	2	0	0
Ghana	8	1	12.50%	Eritrea	2	0	0
Comoros	4	1	25.00%	Congo	2	0	0
Mauritius	1	1	100.00%	Gabon	1	0	0
Sierra leone	5	1	20.00%	Zimbabwe	4	0	0
Seychelles	3	1	33.33%	Cameroon	1	0	0
Tanzania	21	1	4.76%	Lesotho	1	0	0
Tunisia	2	1	50.00%	Mali	1	0	0
Uganda	11	2	18.18%	South Africa	5	0	0
Zambia	18	1	5.56%	Nigeria	11	0	0
Brazil	12	4	33.33%	Sultan	8	0	0
Columbia	3	1	33.33%	Algeria	1	0	0
				Kenya	3	0	0
				Madagascar	3	0	0
				Morocco	6	0	0
				Bolivia	1	0	0
				Peru	1	0	0
				Venezuela	3	0	0
				Chile	2	0	0
				Argentina	4	0	0
Total	117	20	17.09%		55	0	0

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

The area distribution of YFV antigen detection

The YFV antigen detection rate in African was 10.96%, while that in South American was 15.38%. The YFV antigen detection rate of South American was higher than that of African, but the difference was not statistically significant (χ^2=0.1, P=0.752). The YFV antigen was detected in people from 13 African counties out of 31, with 41.94% positive rate, and 2 South American countries out of 7, with 28.57% positive rate. Hence, there was also no significant difference in the detection rate of national distribution (χ^2=0.051, P=0.822). As shown in Tables 1 and 2.

Feature	Number	Constituent ratio	Positive number	Positive rate
Area				
Africa	146	84.88%	16	10.96%
South America	26	15.12%	4	15.38%
x^2 value				0.1
P value				0.752
National distribution				
Africa	31	81.58%	13	41.94%
South America	7	18.42%	2	28.57%
x^2 value				0.051
P value				0.822
Sex				
male	137	79.65%	16	11.68%
female	35	20.35%	4	11.43%
x^2 value				0
P value				1
Age				
<20	12	6.98%	2	16.67%
20-30	49	28.49%	7	14.29%
30-40	82	47.67%	6	7.32%
>40	29	16.86%	5	17.24%
x^2 value				3.006
P value				0.391
Occupation				
contract workers	17	9.88%	5	29.41%
students	91	52.91%	10	10.99%
Technical personnel	64	37.21%	5	7.81%
x^2 value				6.175
P value				0.046
Time				0.289

First and second quarter	36	20.93%	2	5.56%
Third quarter	49	28.49%	5	10.20%
Fourth quarter	87	50.58%	13	14.94%
x^2 value				3.68
P value				0.159
Total	172		20	11.63%

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

The gender distribution of YFV antigen detection

YFV antigen detection rate in male was 11.68%, while that in female was 11.43% among entry-personnel. However, there was no significant difference in detection rate (χ^2=0, P=1), for details see attached Tables 2.

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 17.28%, the positive rate of 30-40 age group was lowest, up to 7.32% through comparing differences of YFV antigen detection rate among groups. And there was no significant difference in detection rate (χ^2=3.006, P=0.391), for details see attached Tables 2.

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 29.41%, the positive rate of technical personnel was lowest, up to 7.81% through comparing differences of YFV antigen detection rate among groups. And the detection rate was statistically significant differences (χ^2=6.175, P=0.046), for details see attached Table 2.

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 14.94%, and there was no significant difference in the detection rate among other groups, for details see attached Table 2.

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 [7]. Between 1996 and 1999, four fatal cases occurred in unvaccinated travelers from the USA and Europe to Brazil (two cases), Venezuela, and Côte d'Ivoire [8]. 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 [9]. 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 [10]. 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 [11,12]. In order to eliminate the influence of cross antigen, the YFV antigen-positive samples were detected for dengue virus and west Nile virus antigen. Based on the experimental results, 2 cases out of 20 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 YFV in 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 [13]. In 2013, 5 immigrants without yellow fever vaccination certificate were found and the YF antigen detection of sera were all negative [14].

In our study, based on the result of area distribution of YFV antigen detection, the positive rates of Africa and South America were 10.96% and 15.38%, 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 42% of African countries and 29% South American countries were detected positive. And no statistical difference was found. The YFV antigen detection rates of male and female were 11.68% and 11.43%, 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, 30-40 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 the viral 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 the quarantine 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 [15].

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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