



INFLUENZA VIRUS UNDERGOES NEW MUTATION- TO H7N9

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ABSTRACT

In the year of 2013, in China, in human infections, the influenza A virus (H7N9) was diagnosed for the first time, which is a subtype of influenza A virus, of avian origin. Since its discovery, this virus has caused a large number of cases of the disease, thus aiming to gather important information about this virus, such as its occurrence and epidemiology, a descriptive study was developed, from the cases of development of Influenza A H7N9, reported throughout the world, observing the zoonotic characteristics presence. From the analyzes made, it was observed in the period from 2013 to 2015, a total of 571 confirmed cases, with 212 deaths, coming mostly from China, where the infected humans, would have entered into contact with the virus, by exposure to poultry, or poultry commercialized live in markets. So far there are no descriptions of cases of infection by the Influenza A (H7N9) in humans and poultry in Brazil.

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INTRODUCTION

Influenza A virus (H7N9) is part of a subgroup of the influenza virus that normally circulates among the poultry, but that can also be transmitted to humans (BRAZIL, 2016). Recent discoveries of infections by the influenza A virus (H7N9) in human patients severely sick, alert its importance to public health (UYEKI *et al.*, 2013). The disease is worrying, because it has been fatal in most cases. Many studies have been performed in the search for information of possible transmissions among humans, zoonotic potential and epidemiological cycle of this disease (BRAZIL, 2016). The key question for the assessment of the risk of a pandemic, is to determine if there are evidences showing limited transmission, or more importantly, from human to human, the latter being indicative of an emerging pandemic (UYEKI *et al.*, 2013), but there are still no evidences of this direct transmission from person to person (BRAZIL, 2016). If the direct transmission is confirmed, the dynamics and modes of transmission, the basic reproductive number and the incubation period should be determined.

For this reason, it is important to determine the disease spectrum, which will help understand the scope of the problem, allowing to assess its severity (UYEKI *et al.*, 2013). It is believed that the first cases of avian influenza A (H7N9) were detected in poultry in March 2013, with no previous records of occurrence of this disease (WHO, 2017). However, since then, infections in humans and birds were observed, making this disease worrying, because it is a hazard to the public health and by the high virulence presented in the majority of patients. In most cases, the human infection caused by avian virus occurred due to recent exposure to live poultry, or potentially contaminated environments, especially markets where live poultry are sold (WHO, 2017). According to data presented in Brazil (2016), there were a total of 571 cases of the disease, confirmed by the world, and of these, 212 have evolved to death. Of this total, 568 cases are from China, a case in a Chinese traveler reported in Malaysia, and two travelers in Canada. There are no cases of the disease in humans and birds, reported in Brazil, until the moment. The objective of this paper is to gather important information about the Influenza A virus (H7N9), its occurrence, epidemiology, and the cases already reported, so that it is possible to obtain greater understanding regarding this new type of Influenza,

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with the purpose of disseminating this knowledge. To ensure that the possible prophylactic measures are imposed, in case there is the development of the disease outbreaks in Brazil.

MATERIAL AND METHODS

A descriptive study was developed on the cases of disease development, caused by Influenza A H7N9, notified by the whole world. Analyzing the origin of the cases, of the disease from the year of its discovery. Furthermore, cases of the disease were analyzed in poultries, and the cases that occurred in humans, noting their relationship and involvement among these species, observing the presence of zoonotic characteristics. As well as prophylactic measures of healthiness and collaboration with animal health organizations. It is also reported, more significant data on the epidemiology of this disease around the world in recent years.

RESULTS AND DISCUSSION

Influenza A virus (H7N9), is a subtype of influenza A virus, of avian origin. This viral subtype (H7N9) had not been detected circulating in animals or infecting humans until the period of March 2013, when cases of human infection in China were first detected (BRAZIL, 2016). Since then, infections in poultries and humans have been observed. There is a great deal of concern regarding human infection with this subtype A (H7N9), because the majority of affected patients developed the flu with severe complications, where the clinical case had progression to death in approximately one third of the cases (BRAZIL, 2016). The avian influenza virus usually circulates among the poultries. Although there are already some known H7 avian viruses, such as (H7N2, H7N3 and H7N7), the H7N9 virus was discovered recently, and has already presented in addition to cases in poultries, cases of humans infection, characterizing this disease as a zoonosis (WHO, 2017). Data on the hemagglutinin sequence (HA) suggest that H7N9 virus are viruses of avian influenza virus of low pathogenicity and that infection of wild birds and domestic poultries will result, therefore, in an asymptomatic or moderate disease in this species (UYEKI *et al.*, 2013).

The virologic and epidemiological information, strongly indicate that the majority of known human infections caused by H7N9, derived from direct or indirect contact with infected poultries, the exposure to broilers, or with potentially contaminated environments, such as the trade in live poultries. The fact of the infections caused by H7N9 do not cause serious disease in poultries, this infection can spread "silently" in the animal species, and cause infections more easily in humans. The World Health Organization (WHO) and the animal health partners monitor the virus continuously throughout the world (WHO, 2017). In the period from 2013 until 2015, there were a total of 571 confirmed cases of H7N9, with 212 deaths, coming mostly from China (BRAZIL, 2016). Some studies have indicated that the avian influenza virus, as well as the seasonal influenza virus, have a pattern of seasonality: they circulate with high rate during the cold climates and with low rate in hot climates (BRAZIL, 2016). The first identified cases of human infection with new influenza A virus (H7N9) occurred in the eastern part of China during February and March 2013 and were characterized by pneumonia of rapid progression, respiratory insufficiency, acute respiratory distress syndrome and death (Li *et al.*, 2014). From 1996 to 2012, human infections were reported with avian influenza

virus H7 (H7N2, H7N3 and H7N7) in Canada, Italy, Mexico, the Netherlands, the United Kingdom and the United States of America. The majority of these infections occurred in association with outbreaks of poultries. The infections resulted mainly in conjunctivitis and mild respiratory symptoms in upper tract in humans, and that may come to death, as well as in a case that has attacked a Veterinary Doctor in the Netherlands, caused by these other variants of the avian influenza virus (WHO, 2017). This new influenza A virus (H7N9), is associated with severe human infection. Currently, only 25 H7N9 virus are available at Gen Bank. The H7N9 virus identified in three patients were of avian origin, but only the gene NA was closely linked with that of other virus H7N9. The gene HA was similar to that of a virus H7N3, from a closer region (Zhejiang Province) in China. All internal genetic segments were closely related to the avian virus H9N2 (Rongbado *et al.*, 2013). The geographical distribution of the virus has affected, locations, such as: China, Taiwan, Hong Kong, Malaysia, Canada. The current data for Influenza A (H7N9), indicate that the incubation period varies from 2 to 8 days and may reach up to 10 days. OMS informs that in field studies, the patients showed an average incubation period of seven days (BRAZIL, 2016). Despite the period of transmissibility in humans is unknown for this new virus, usually an adult releases viral particles from one day prior to the onset of symptoms, up to five to ten days after the onset of symptoms (BRAZIL, 2016). According to Brazil (2016), the clinical manifestations presented by patients with confirmed infection by influenza A (H7N9), during hospital admission, include fever, productive and non-productive cough, dyspnea, hypoxia, evidence of respiratory disease of the lower tract with opacity, consolidation and infiltrates in pulmonary images. The leukocyte count has been normal or low, with leukopenia, lymphopenia and thrombocytopenia in some cases.

Complications caused by infection with the Influenza A virus (H7N9) include septic shock, respiratory failure, acute respiratory distress syndrome, refractory hypoxemia, renal failure, multiple organ failure, rhabdomyolysis, encephalopathy and secondary bacterial infections (BRAZIL, 2016). According to a study performed by Li *et al.* (2014), the transmission of H7N9 virus from humans to humans, has still not been confirmed, but this possibility of virus transmission is not discarded. The majority of patients with confirmed infections caused by Influenza A (H7N9), need hospitalization in intensive care unit. The average time of onset of symptoms until death is approximately 11 days, and can vary from 7 to 20 days. The evolution to death occurs in about 30% of the cases (BRAZIL, 2016). According to data of the confirmed cases, March 25th to December 1st 2013, which respiratory samples were tested of 1372 patients hospitalized with pneumonia of unexplained origin, 104 patients (7.6%) were diagnosed with the infection by the virus H7N9. Of the 2,130,049 respiratory specimens obtained from ambulatory patients with flu disease through the sentinel surveillance system for influenza-like illness, 8 (0.0004%) were positive for H7N9 virus (Li *et al.*, 2014). Just as the Influenza virus H7N9, there are studies that show that other subtypes of influenza, such as H5N1, where the poultries are also virus transmitting to humans, according to a study performed by Dinh, P. N. *et al.* (2006), where in the period of 2004 in Vietnam, there were 28 confirmed cases in humans, out of 106 respondents. From December 1st 2013, a total of 139 confirmed laboratory cases were identified of infection by the virus H7N9 and 1 suspected case. Cases were identified in 10 provinces and 2

municipalities: Zhejiang (50 confirmed cases), Shanghai (33 confirmed cases and 1 suspected case), Jiangsu (28 confirmed cases), Jiangxi (6 confirmed cases), Fujian (5 confirmed cases) and 1 case in Hong Kong. The mean age of the patients with confirmed infection by H7N9 virus was 65 years, where 58 cases, or 42% occurred in persons with 65 years of age or older, and 43% in children younger than 5 years of age, all with upper respiratory disease clinically mild (Li *et al.*, 2014). In these cases, 71% occurred in men, 73% of the patients were urban residents and 79 (73%) of 108 patients with data available had underlying medical conditions. In 70 of 79 patients with sufficient data to a more specific classification of the underlying conditions, 54, or 77% were considered as having an increased risk for flu complications due to age (<5 years or ≥65 years) (Li *et al.*, 2014). According to Li *et al.* (2014), of the patients with confirmed cases, 9 worked as poultry farmers. A total of 137 of the 139 patients with confirmed infection by the virus H7N9 (99%) were hospitalized, and 125, or 90% had pneumonia or respiratory insufficiency. Among the 103 patients with confirmed cases for which data were available, precautions have been taken in isolation for around 65% of them, who went to the ICU because of severe disease of the lower respiratory tract. Among the patients with identified cases from December 1st, a total of 47 people (34%), with confirmed infection by the virus H7N9, who died due to (ARDS) or multiorgan failure in the hospital, 2 critical patients with confirmed cases remained hospitalized, 88 were discharged, and a person was suspected of this infection. A 2-year-old child a 25-year-old woman with mild disease of the upper respiratory tract were not hospitalized.

Among the 139 confirmed cases of infection by the virus H7N9, 49, or 35% were confirmed by isolation of the virus, 1 through serologic tests and 89, i.e., 64% by detection of viral nucleic acid (LI *et al.*, 2014). The 5 persons, of 139 with Virologically confirmed cases, also were seropositive for antibodies to virus H7N9, with the use of a haemagglutinin inhibition test of turkey's red cells. The data on recent exposure to animals were available for 131 of the 139 patients with confirmed infection by the virus H7N9. Of these, 107 (82%) reported a recent history of exposure to animals, and 88 (82%) for chickens, 24 (22%) for ducks and 6 (6%) for pigs. The exposures occurred while they were working somehow with birds, or while they were visiting a market of live birds (LI *et al.*, 2014). If the infection with the H7N9 virus is mainly zoonotic, as the studies so far suggest, it is assumed that the transmission occurs through exposure to asymptomatic poultries, in contrast with the infection caused by the virus H5N1 (UYEKI *et al.*, 2013). In poultries infected by this virus, major economic losses are not observed, as opposed to what occurs with infection by the virus H5N1, where the vast majority of cases, there is a rapid death in infected chickens (UYEKI *et al.*, 2013). Other animals to which the 107 patients reported having been exposed, include pigeons, geese, quail, wild birds, pet birds, cats and dogs. The information about the history of exposure to animals is not clear for 8 patients with confirmed infection by the virus H7N9 (Li *et al.*, 2014). On May 9th, WHO had reported 131 confirmed cases by laboratory. In these cases, lymphocytopenia was observed in 88.3% of the patients and thrombocytopenia in 73.0%. The treatment with antiviral drugs was initiated in 108 patients (97.3%) on average 7 days after the disease onset (GAO *et al.*, 2013).

Currently, there is no vaccine for the prevention of infection by H7N9 in humans. WHO has been working with its partners for the development of vaccines and some products have already being tested for safety and efficacy (BRAZIL, 2016). Laboratory tests show that antiviral drugs, called neuraminidase inhibitors are effective against flu H7N9. Among people infected with H7N9 in China, in some of the patients who received early treatment with neuraminidase inhibitors, it was observed with a milder disease than those treated later (BRAZIL, 2016). The world health authorities guide the following measures: Enhanced surveillance for cases of pneumonia of unknown origin to ensure early detection and laboratory confirmation of new cases, epidemiological research, including the assessment of suspected cases and contacts of known cases, and close collaboration with animal health organizations to determine the infection source (BRAZIL, 2016).

Conclusion

It is concluded that this is an important zoonosis, which requires more detailed studies, in order to obtain greater knowledge about this new type of influenza so that we are prepared and aware of the risks that this virus represents. It is very important that the authorities and all sectors linked to health in Brazil, have knowledge of this disease and know what control and prevention measures can be taken if cases of the disease in Brazil occur, because it puts at risk the country's public health. The enhanced surveillance of infection by the virus H7N9 is therefore urgently required among patients hospitalized and ambulatory patients of all ages with less severe respiratory diseases, to make the monitoring of suspected cases.

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