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Original Article

Surveillance of Use of HIV Combined Ag/Ab Assay in Taiwan

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Abstract

The Human Immunodeficiency Virus (HIV) is a type of Retrovirus which can induce the Acquired Immune Deficiency Syndrome, also referred to as AIDS. Currently, medical testing facilities in Taiwan mainly use the Enzyme Immunoassay (EIA) as the test reagent for detecting HIV infections and the Particle Agglutination (PA) for detecting HIV antibodies in determining whether an individual is infected with HIV. The newest generation of HIV antigen/antibodies combined reagents can simultaneously detect not only HIV antibodies but also the p24 HIV antigen, and in doing so they help reduce the HIV testing window period. According to questionnaire data compiled by the Taiwan Society of Laboratory Medicine (commissioned by this Center), the number of facilities using the HIV Ag/Ab combined reagent was 49 in 2009 and increased to 91 in 2010; by 2011, the numbers of facilities using this reagent had reached 130. This reflects the increasing importance placed on HIV detection by medical testing facilities in Taiwan. The continuous improvement in testing efficiency shortens the HIV testing window period, leads to earlier detection of HIV, and aids in preventing further spread of the virus. However, the sensitivity is not as high as NAT and thus has its limitations when detecting acute HIV infections

Key words: HIV, AIDS, antibody testing, antigen testing, combined testing reagent

Introduction

HIV can be transmitted through blood or semen. After a person is infected by HIV, the virus can spread through the whole body through the blood stream, leading to infection and destruction of immune system cells and lowering the immune system function; the

ensuing disease stage where random opportunistic infections appear and induce a breakdown of the immune system is called Acquired Immunodeficiency Syndrome, commonly referred to as AIDS. This disease is characterized by acquired deficiencies of the immune system that make an individual vulnerable to opportunistic infections that can be fatal[1-4]. In 1981, the first case of AIDS was discovered in the US, and the disease has developed into a worldwide epidemic in the following decades. According to data from the Joint United Nations Programme on HIV/AIDS (UNAIDS), by the end of the year 2010, approximately 34,000,000 of the world's population have contracted HIV[5]. In Taiwan, after the first case of AIDS was found in a foreign national and reported in 1984 and the first local case of HIV infection was diagnosed in 1986, the number of HIV cases in Taiwan gradually climbed up in the following years. By the end of 2011, the number of HIV cases had reached 22,822[6] in Taiwan according to data from the Centers for Disease Control.

During the initial period of HIV infection when HIV antibodies have yet to be produced, there are currently two methods that can be used to detect HIV infection, which help shorten the testing window period. One of these methods is Nucleic Acid Testing (NAT), and the other is by testing for HIV antigens in serum or plasma[7-9]. Among HIV antigens, the antigen most frequently used to test for early infection is the structural antigen p24. Considering the operational standards and costs, most medical testing facilities use methods that simultaneously detect HIV antigens and antibodies to shorten the HIV detection window period.

In 1985, the first-generation HIV antigen testing reagent was developed; this reagent uses the whole virus as antigen to test for the HIV IgG antibody within the body. Later, due to the lack of sensitivity and specificity of this test, the second-generation reagent was developed in 1987, which mainly tests for the HIV IgG and IgM antibodies. After the appearance of a HIV-2 infection case, a third-generation reagent was developed in 1994 to test for HIV-2. Due to the continuous development of testing technology, a fourth-generation reagent was developed in 1997 to test for both HIV antigens and HIV antibodies; the main difference between this reagent and the third-generation reagent is that apart from testing for HIV antibodies, the p24 HIV antigen can also be tested for simultaneously. This antigen can detect both HIV p24 and HIV antibodies in the initial HIV infection period when HIV antibodies have not yet been produced or appeared within the human body. Compared with detection of only HIV antibodies, this can effectively reduce the HIV testing window period (Figure 1) [10-11.]

Laboratory test results provide an extremely important reference in the prevention of AIDS. Quick and correct test results can aid in finding HIV infected cases and lower the chance of HIV transmission when proper health education and medical assistance are provided to HIV infected individuals. This can effectively prevent further spread of HIV and serve the goal of epidemic control. In Taiwan, medical testing facilities which

perform HIV testing differ in size, testing methods and equipment. Therefore, their testing results also differ in accuracy and sensitivity. In order to understand the situation of HIV testing reagent use in medical testing facilities in Taiwan, we commissioned the Taiwan Society of Laboratory Medicine to conduct a survey with each of the medical testing facilities that engage in HIV testing and its promotion. This survey would help shed light on the current situation of HIV testing in medical facilities in Taiwan and provide an important reference for monitoring and improving testing quality in the future.

Materials and Methods

Research Subjects

This study involves all levels of medical testing facilities in Taiwan that provide AIDS or viral hepatitis testing. These include Health Centers in each county/city, designated hospitals for foreign workers, anonymous AIDS screening hospitals, drug-addiction monitoring facilities, pregnant women AIDS screening projects, medical testing facilities, military personnel health checkups, and blood donation/use facilities, all of which were listed as questionnaire investigation subjects. A list of contact information of 2,318 medical facilities was compiled, and questionnaires were sent to them during the years between 2009 and 2011. Using self-report, the type of testing reagent and other relevant data were investigated.

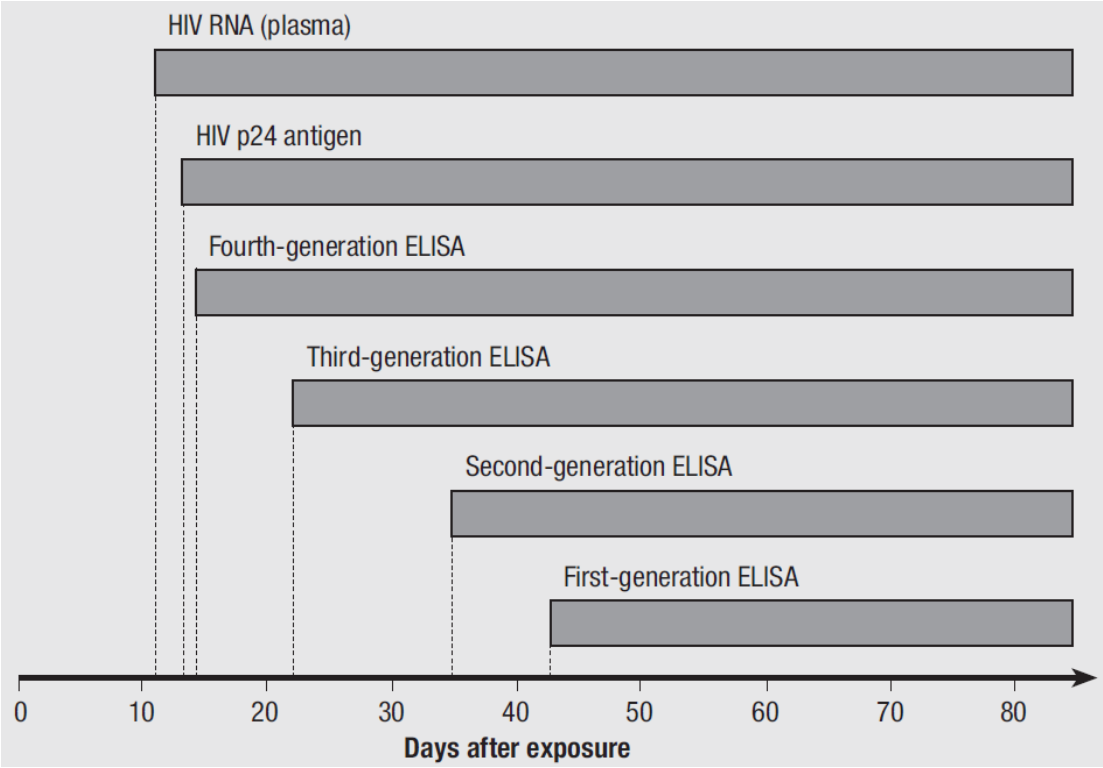

Figure 1. The Development of HIV Testing Reagents and Special Markers (Figure from Stefano Buttò, Barbara Suligoi, Emanuele Fanales-Belasio and Mariangela Raimondo. Laboratory diagnostics for HIV infection. Ann Ist Super Sanità 2010, 46:24-33)

Results

1. Descriptive statistics of medical testing facilities which run HIV antibody screening in Taiwan

Seven hundred and twenty-four effective questionnaires were completed and returned in 2009, 666 in 2010, and 616 in 2011, which translated into an average response rate of 45.68%. Among the effective questionnaires of 2009, 391 facilities provided the public with AIDS screening tests, constituting 54.01% of the effective questionnaires; in 2010, there were 389 facilities, constituting 58.41% of the effective questionnaires; in 2011, 379 facilities were documented, constituting 61.53% of the effective questionnaires; the average response rate was 57.98%. Telephone interviews were conducted with a sample of those facilities that did not return the questionnaire. The results of these telephone interviews showed that those facilities either did not conduct AIDS/viral hepatitis testing or had their tests commissioned to other facilities. Among those medical testing facilities that conducted HIV antibody screening, medical testing facilities constituted the largest group, followed by local hospitals, and local teaching hospitals (Figure 2).

2. Investigation of current HIV antibody screening situation

According to law, the reagents used by medical testing facilities must have a medical equipment approval certification issued by the Food and Drug Administration, Department of Health. Until 2011, manufacturers who had received a certification to manufacture HIV antibody screening reagents included: ABBOTT, ROCHE, FUJIREBIO, SIEMENS, BIO-RAD,

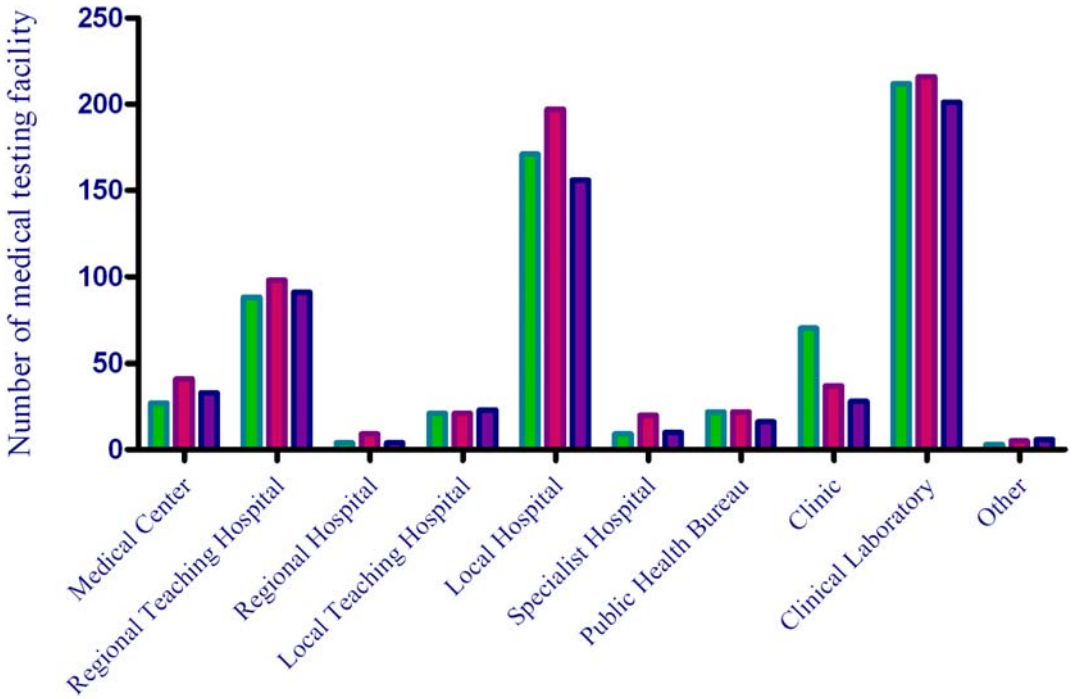

Figure 2. Statistics of Medical Testing Facilities in Taiwan which Conduct HIV Antibody Screening. Green columns show the number of medical testing facilities that conducted HIV antibody screening in 2009, Red columns show the number of facilities in 2010, and Purple columns show the number of facilities in 2011

GENERAL BIOLOGICAL, MUREX BIOTECH, and ORTHO-CLINICAL. The main principles behind HIV antibody screening test can be categorized into two types of methods—Enzyme immunoassay (EIA) and Particle agglutination (PA). Those number of medical testing facilities that used EIA was 240, 262, and 271 in 2009, 2010, and 2011, respectively; those medical testing facilities that used PA to screen for HIV antibodies numbered at 156, 149, and 150 in 2009, 2010, and 2011, respectively.

According to the survey data collected from 2009 to 2011, in 2009, 49 facilities used HIV Ag/Ab combined reagents, which constituted 20.4% of EIA screening facilities. In 2010, this number increased to 91 facilities, which constituted 34.7% of EIA screening facilities. By 2011, 130 medical testing facilities were using HIV Ag/Ab combined reagents, which constituted 48.0% of EIA screening facilities (Figure 3). This shows the increasing importance placed upon HIV testing by Taiwan's medical testing facilities. Through continuous improvement in testing effectiveness to reduce the HIV testing window period and to detect HIV infected cases earlier, further spread of HIV infections can be effectively controlled.

Discussion

According to results from a survey conducted between 2009 and 2011, medical testing facilities at various levels, such as medical testing centers, clinics, specialist hospitals, local hospitals, regional hospitals, and medical centers, all had units that provided the public with AIDS virus antibody screening tests. Apart from this, government units, including county/city

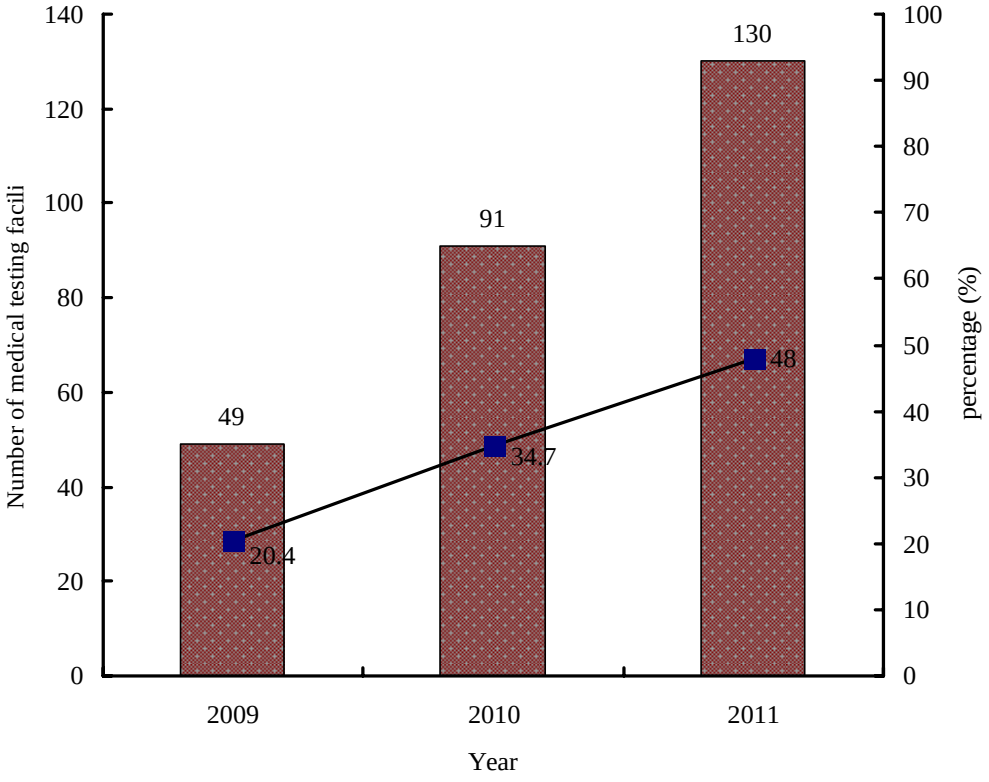

Figure 3. Statistics of Medical Testing Facilities in Taiwan which Use HIV Ag/Ab Combined Reagents. The percentages shown are of the use of HIV Ag/Ab reagents among those facilities which use EIA screening.

health centers, also provided such testing. According to the data collected in 2011, there are currently 380 facilities that provide AIDS antibody screening, most of which use the EIA method, followed by the PA method. In addition, the number of medical testing facilities using EIA is increasing; the main reason may be that tests using the EIA reagents can be conducted with automatic equipment, making them more convenient and leading to a higher inclination to use this method. Among those medical testing facilities that run HIV antibody screening, most are medical testing centers, followed by local hospitals, regional teaching hospitals, and medical centers. This shows that the base-level medical testing facilities place much importance on the screening for AIDS antibodies and therefore are willing to provide such service to the public at many testing stations, which greatly aids HIV prevention.

The issue of how to reduce the HIV testing window period has been extremely important; under budgetary, man-power, equipment and other practical considerations, using NAT to test for HIV enzymes to reduce the HIV testing window period is currently still difficult due to cost, technology, and equipment limitations. Therefore, a testing method which is easier to carry out and does not need expensive equipment to run tests (i.e. the fourth-generation HIV combined testing reagent) is more suitable for the current situation. This type of reagent not only tests for HIV antibodies, but also for HIV antigens (p24), which is a great aid in shortening the HIV testing window period and is also much more budget-friendly than HIV enzyme testing methods; thus, there has been a continuous increase in the number of medical testing facilities that choose this type of testing method. However, although the cost is lower with this type of testing reagent, the sensitivity is not as high as NAT and thus has its limitations when detecting acute HIV infections. When medical testing facilities used reagents to test for HIV antibodies in the past and the results come up positive, further testing using Western bolt (WB) was used to confirm whether the HIV antibody was positive or not; if the WB results turned out to be negative, the final test results was labeled to be negative. However, when using the newest generation of HIV Ag/Ab combined testing reagent, which can detect HIV antigens, if the results are positive, this shows that the production of either HIV antibodies or HIV antigens is positive. During the window period of acute HIV infections where antibodies have not yet been produced and only antigens exist, if test results using the Western Blot method are negative, the possibility of positive HIV antigens still needs to be considered, and the traditional diagnostic habit of concluding the final test result is HIV negative should be discontinued. This is an understanding that testing facilities and clinicians need to acquire when using the new generation HIV Ag/Ab combined testing reagent in order to bring this new generation reagent into full play.

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Outbreak Investigation Express

A vaccine adverse event associated with seasonal influenza immunization in central Taiwan, Oct 2012

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Abstract

Trust in vaccine safety is a major issue in influenza vaccine campaign. To maintain the public trust, investigating the nature of vaccine associated adverse event promptly is essential. An 11-month-old female infant died suddenly one day after influenza immunization on October 5th, 2012. The Public Health Bureau of Taichung City Government visited the family immediately to offer assistance. The forensic examination performed by Taichung District Prosecutors Office (TDPO) and the Institute of Forensic Medicine (IFM) revealed signs of cardiomegaly and lung consolidation. Taiwan Centers for Disease Control, commissioned by IFM, detected Parvovirus B19 viral DNA in the infant's body. The pathological findings and laboratory results showed the infant was died of Parvovirus B19 associated severe subacute lymphocytic myocarditis. The infant's family was informed of the forensic diagnosis by the TDPO on October 12th and the investigation report was released on October 13th. Our report illustrated the proactive strategies in managing the vaccine adverse event. The sophisticated collaboration between public health authority and judicial authority is crucial in averting a vaccine associated public trust crisis.

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