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Open Access Journal of Gynecology
ISSN: 2474-9230

Accuracy of a Dual Test for Detection of HIV1 and Syphilis at an Urban Hospital in Kampala- A cross-sectional study

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Investigation Paper

Volume 5 Issue 1

Received Date: March 13, 2020

Published Date: April 22, 2020

DOI: 10.23880/oajg-16000190

Abstract

Background: Dual rapid point of care test kits for multiple infections such as HIV and syphilis can greatly improve the screening and detection of such infections in vulnerable groups.

Methodology: A cross sectional study was conducted at St. Francis Hospital Nsambya ante natal clinic between 16th March and 3rd May 2015. All pregnant women attending the clinic for the first time were screened and eligible participants enrolled in the study after informed consent. Data was collected using structured questionnaire; whole blood was collected from participants by venapuncture. Data was entered into Epi data version 3.1 analysed with IBM SPSS version 16.

Results: A total of 549 were screened for the study and 476 (86.7%) were tested for HIV and syphilis. Fifty two had already tested for HIV and syphilis and 21 left the clinic without being tested. Of those tested 9 had inconsistent data and 5 did not have confirmatory results due to mis- identification. Only 462 (84%) results were available for analysis. The sensitivity and specificity for ASTEL HIV and syphilis was 79% and 77% respectively. The PPV and NPV for ASTEL kit for HIV and Syphilis was 99%, 92 and 99, 93% respectively. The sensitivity /specificity/PPV and NPV for Determine HIV were 74%/100%/99% and 89% 38%/98%/96% and 92% for syphilis. The prevalence of HIV in the study was 4%, C.I 2-6% while that of syphilis was 6 %, C.I 4-8%.

Conclusion: The sensitivity of the ASTEL kit for HIV and syphilis was lower than that given by the manufacturers and other laboratory based studies but was better than that of the routine Determine tests. The low prevalence of HIV and syphilis in this study population may have resulted in a higher proportion of false negatives hence affecting the positive and negative predictive values

Keywords: HIV; Syphils; ASTEL Kit; Dual testing

Background

About 1.5 million pregnant women were infected with(Human Immunodeficiency virus type 1(HIV-1) in 2013 [1] and only 35 percent of women (up from 8 percent in 2005) were estimated to have been tested for HIV [2]. Mother-to-child transmission of HIV (MTCT) contributes 16, 000 (11 percent) of an estimated 145,000 new infections occurring each year. To curb the MTCT of HIV rate, HIV must be diagnosed and appropriate treatment and care must be provided [2].

Syphilis prevalence was estimated to be between 2.5 percent to 17 percent among pregnant women attending antenatal care in Sub-Saharan Africa [3] and was found to be 4.3percent in the Ugandan fishing community and 3-18percent among pregnant women [4,5]. Syphilis can seriously complicate pregnancy and result in spontaneous abortions, still birth, intra uterine growth restriction and perinatal death [6]. HIV and Syphilis co-infection in

pregnant women increases the risk of MTCT as compared to pregnant women with HIV alone [6]. Therefore, to achieve dual elimination of these serious infections [2] all pregnant mothers need to be tested for HIV and Syphilis as recommended by WHO.

The MDG Goal 6 focused on elimination of HIV, although this was not achieved by Uganda [7] to achieve Sustainable Development Goal 3, a continuation of the MDGs goal 4, 5 and 6, that ensures and promotes good health for all persons; screening for HIV and syphilis should be emphasized in all health care facilities.

Screening for HIV and Syphilis during pregnancy is a policy in Uganda although implementation is still a challenge in some areas [5,6]. The routine tests used in the ANC are performed separately and are not as accurate as they should be [8]. Determine, which is the commonest type of rapid test used in Uganda has a failure rate of 5% for correctly identifying HIV persons as HIV positive. Therefore there is a proportion of babies born to HIV positive mothers that are unprotected (MOH unpublished Data)

Several dual rapid Point Of care (POC) tests have been experimented and WHO is promoting evaluation and use of multiple infection detection tests, although few have been tested in the field [2]. A single dual rapid test that would test both HIV and Syphilis would reduce on the waiting time and the number of women who walk away without getting their results.

Simultaneous testing for HIV and syphilis would not only be cost effective, but also reduce the number of women who would otherwise miss out on testing due to stock outs [9]. Dual tests have also been found to be simpler and more convenient to the users as well as requiring less volumes of blood [10].

However, none of these tests has either been evaluated extensively or approved for use by Ministry of Health as part of the Ugandan Algorithm for HIV testing. Therefore, health facilities in Uganda including ante natal clinics still use still use separate tests for HIV and Syphilis without carrying out confirmatory tests.

The ASTEL kit (ASTEL diagnostics, Kampala) was evaluated in the laboratory as a dual rapid Point of Care test for HIV and Syphils (POC) using samples obtained from sera of known HIV and syphilis status with sensitivity and specificity of 100%. It is a rapid immunochromatographic direct binding test for the visual detection of anti-HIV antibodies and anti-TP antibodies in whole blood, serum or plasma samples. It employs the double antigen sandwich method. When the specimen is added into the test device, the specimen is absorbed into the device by capillary action, mixes with the antigen-dye conjugate, and flows across the pre-coated membrane. However, its effectiveness in the field especially among pregnant women remains unknown.

We evaluated the accuracy of a dual test for detection of HIV 1 and syphilis at an antenatal clinic in one of the suburbs of Kampala city, Uganda. We used ELISA HIV IgA/IgG for HIV and Treponema Pallidum Particle Agglutination for syphilis as reference standards [11,12]. The aim of the study was to evaluate the accuracy of this dual test for HIV and syphilis screening among pregnant attending the antenatal clinic for routine prenatal care.

Methods

St. Francis Hospital Nsambya antenatal clinic Kampala, Uganda from March to May, 2015 venous blood samples were collected into EDTA tubes from a convenient sample of pregnant women at their initial antenatal visit.

This study was approved by the Institutional Review Board of the hospital and all participants signed a written informed consent. All pregnant women having their index visit to the clinic and were 18years and above and well were invited to participate in the study.

Sample collection, handling and processing was done laboratory technicians at the hospital laboratory but confirmatory testing was done at Medical Research Council laboratory using plasma stored at -80°C. Using manufacturer's instructions, the kit was kept at a room temperature between 20-30°C. The test cassette was removed from the foil pouch by tearing at the notch and placed at leveled surface. Whole blood was collected from participants by venapuncture. It was centrifuged at 3500rpm for 3 minutes to obtain serum. 10ul of serum was slowly added to the sample well. Two drops of dilution buffer was added to the buffer well purple color was observed across the result window in the centre of the test device. The results was read after 15minutes [13]. ELISA (vironostika HIV UniformII antigen/antibody Biomerieux, the Netherlands) and Triponema Pallidum Particle Agglutination (Serodia, Fugirebo) were the gold standands for HIV and Syphillis respectively.

Data was double entered in Epi data version 3.1 and analyzed with IBM SPSS version 16. Numerical discrete and categorical data was grouped and analyzed. The means and categories for Age, parity, gravidity, and effect on test result were analyzed. The sensitivity, specificity, positive and negative predictive values were calculated using the standard formula as elaborated below. Pearson Chi square for categorical data was obtained.

Results

A total of 549 were screened for the study and 476 (86.7%) were enrolled with a mean age of 28(SD5) for HIV and Syphilis. Of those screened, 52 mothers had already tested for HIV and syphilis and had results from a recognized facility and 21 left the clinic without being tested. Out of those tested, 9 had inconsistent data and 5 did not have confirmatory results due to misidentification. Therefore, a total of 462 (84%) results were available for analysis. Out of the 462 analyzed 19(4%) were HIV positive, 26(6%) syphilis positive and 3(0.6%) were co - infected with HIV and syphilis. The average gestational age was 21±7 and most women were nulliparous with a mean parity of one. Only one percent of the participants were on medication at the time of the study and 2 percent had suffered a febrile illness in the past one month (Table 1-Table 4).

Variable	Mean ±SD
Age(years)	28(5)
Gestation(WOA)	21(7)
Gravidity	3(2)
Parity	1(1)
Proportions (%)	
Ever tested for HIV	99
On medication	1.1
History of febrile illness in past 1 month	

N=462.

Table 1: Characteristics of the Study Participants.

		TPPA		
		reactive	**nonreactive**	**Total**
Syphilis	reactive	10	1	11
TPHA	nonreactive	16	435	451
Total		26	436	462

Table 2: Positive and Negative results for ASTEL HIV/Syphilis for syphilis.

		ELISA		
		positive	**negative**	**Total**
ASTEL	positive	15	5	20
HIV	negative	4	436	440
Total		19	441	460

Table 3: Positive and Negative results for ASTEL HIV/Syphilis for HIV.

The ASTEL HIV and Syphilis tests had modest sensitivity of 79% (95% CI: 52 – 90%) and 77% (95% CI: 72-104%), respectively. However, both tests had excellent specificity of 99% (95% CI: 98 – 100%). The ASTEL syphilis tests had a sensitivity of 77% and specificity of 100%.

	Sensitivity (%) %CI	**Specificity(%) %CI**	**PPV (%)**	**NPV (%)**	**%agreement)**	**Kappa coefficiency (CI)**
ASTEL/ELISA	79(52-90)	99(98-100	75	99	92	0.74(5.8-8.9)
ASTEL/TPPA	77(72-104	100(98-99)	74	99	93	0.79 (0.64-0.92)

Table 4: Accuracy of the ASTEL Kit.

Discussion

The sensitivity of the ASTEL for both HIV and syphilis modest at 79 %and 77% respectively but the specificity was excellent at 99% and 100% respectively when tested on pregnant women attending an urban antenatal clinic. Although sensitivity and specificity were far below that reported by the manufactures of 100% this study can be replicated in a larger studies because of the good specifity. The ASTEL may also be used alongside the routine kits as a confirmatory test especially for syphilis.

This being the first field study for this kit, it can only be compared to others kits similar characterists. The STD

Reference Laboratory of the National Center for STD Control, China and the laboratories of the University College Hospital (UCH) in Ibadan, Southern Nigeria, and the Ahmadu Bello University Teaching Hospital (ABUTH) in Zaria, Northern Nigeria performed multisite laboratory tests on dual kits for HIV and syphilis [14]. These laboratory based studies were conducted by Yue Ping et al, 2014 using 1514 stored specimen. SD Bioline had a sensitivity of 98.4 % and specificity of 98-99.5 % and the Chembrio showed an accuracy of 100%. Yue Ping et all evaluated several combined kits in the field their lowest sensitivity for HIV and syphilis were 98-100%and 99-98% respectively [14].

This SD Bioline, was also evaluated study in rural Western Uganda among 220 pregnant women attending a public heath care facility using showed a sensitivity of 100 percent. However, kit was not compared to a gold standard and the prevalence in this population was higher that found in this study [10]. The reading time for this kit is longer than that for ASTEL kit; 25versus 15 minutes.

In their study Hess K.L, et al. [15], used the Dual Path Platform HIV/syphils (DPP) kit with similar characteristic to the ASTEL kit on whole blood specimen. The participants included both men and women; pregnant and non-pregnant attending a who provided the samples were mixed pregnant women and non-pregnant and study was done in long Beach, California USA. Unlike the Ugandan study, the investigators used the same gold standard tests that were used in this study i.e., ELISA for HIV and for syphilis. They found the kit to have a sensitivity ranging from 95-100% and specificity from 99.7-100% [15].

These sensitivity of ASTEL kit for HIV falls far below the target profile minimum 98% and optimum of 99%. The Target Product profile sensitivity recommended by London school of Tropical Hygiene for combined HIV and syphilis is > 98% [16]. This indicated that it did not perform as expected by manufacture. The sensitivity of ASTEL kit for syphilis of 75% achieved the minimum requirement of target product profile for routine tests and had an excellent specificity.

These dual test kits have proven to be superior to the available Determine kits which are currently used some times as sole tests for HIV testing especially in rural health care facilities. The use of Determine alone should be discouraged since it is likely to misclassify some individuals as HIV negative [11]. The Determine TP has an unacceptably low sensitivity of 38% implying that about 65% of pregnant women are misclassified as syphilis negative. These misclassifications are of public health concern since they not only delay initiating medical treatment for these infections but also lead to transmission of the infections to unborn babies.

The ASTEL HIV and Syphilis, had a modest PPV of 75% and 99% respectively and NPV of 99% and 93% respectively when compared to the gold standard. PPV .The PPV and NPV represent the degree to which the test actually predicts the presence of absence of a disease [8]. The PPV strongly influenced by the prevalence of a disease in the study population. Although the national prevalence of HIV in Uganda among adults is estimated to be 7.3%, the prevalence found in this study was 4%. The prevalence of syphilis was 6% which is within the prevalence range for syphilis in Uganda. The lower the prevalence, the more likely the test will have false positives and the higher the prevalence the higher the possibility of a test to have false negatives [17]. The PPV in this study may have been influence by the very low prevalence of HIV in this study population.

This was the first field study to evaluate the accuracy or validity of the ASTEL kit in Uganda which was compared with the standardized laboratory based tests for confirmation of positive results.

This study used venous blood because a large sample was required to carry out other routine tests instead of a finger prick. This prolonged the processing and testing time and may have been a major limitation of the study. The study population is unique (private**,** faith based, more educated) and this may affect the generalizability of the study. The low prevalence of HIV of 4% compared to national prevalence of 7.3% in this population may have influenced the PPV and NPV.

Conclusion

HIV and syphilis contribute significantly to the burden of disease in resource constrained community. There is need to stop the mother to child transmission of these infections. Dual tests provide testing for multiple infections at the same setting and are an effective way of reducing adverse outcomes in pregnancy. The ASTEL kit needs to be evaluated in larger studies and compared to routine tests to assess how they perform in comparison. The low prevalence of HIV and syphilis may have resulted in a higher proportion of false negatives.

Given the simplicity of performing these POC rapid diagnostic tests, they should be rolled out in all health centre especially in the ANC. A multi -site study should be conducted to evaluate the accuracy of this dual test kit. A large multicentre study in a public setting should be conducted to further evaluate the performance of the Aster Kit.

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