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National HIV Testing Algorithm in Ghana – Efficiency and Public Health Implications

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Abstract

Testing and diagnosis of HIV infection is considered an important component of the fight against the pandemic. To achieve this, an algorithm which uses highly sensitive and specific tests must be employed. To assess the efficiency and public health implications of the national testing algorithm used for the screening and diagnosis of HIV in Ghana, a systematic review of the literature on the performances of the First Response and Oraquick Advance HIV-1-2 test kits was conducted. Searches in online journals, credible websites and institutions were done to access evaluation reports on the rapid kits to determine their suitability for use in the algorithm in Ghana. The First Response showed varied sensitivities ranging from 88% – 100% in post- market evaluations done in Ghana. The average specificity was 87.4% (range 82. 56%– 92%) when serum was used as the specimen of choice. One study which used whole blood reported a specificity of 100%, significantly better than those obtained with serum. The only report on the OraQuick produced a sensitivity of 98% and a specificity of 94%, falling short of the WHO's recommended performance characteristics for HIV rapid kits. This study has revealed that the current testing algorithm in Ghana may not be efficient for screening and diagnoses of HIV infections.

Keywords*: HIV, Rapid tests, Testing algorithm, Sensitivity, Specificity.*

Introduction

Testing persons for HIV is important in controlling the impact of the HIV/AIDS pandemic because it allows for counseling and diagnosis of HIV-infected persons (sexual partners and pregnant women) and facilitates the implementation of prevention strategies [Koblavi-Deme et al (2001)]. For instance, in Thailand, Ivory Coast, Burkina Faso, and Uganda, following diagnosis, a short-course regimen of oral Zidovidine or Neviripine administered to HIV –infected pregnant women was found to reduce the rate of transmission of HIV-1 from infected mother to child by 38 to 50% when given within clinically relevant time [Koblavi-Deme et al (2001)]. Studies have also demonstrated that many infected persons reduce behaviours that transmit infection to sex or needle-sharing partners once they are aware of their positive HIV status whereas infected persons who are unaware of their infection do not reduce risk behaviours [The Body]. The World Health Organization (WHO) encourages the use of rapid tests which will prove crucial in achieving the 90-90-90 target of the organization, especially in resource-poor settings. Many HIV rapid diagnostics kits have flooded the Ghanaian market and false outcomes have serious implications on the health and mental well-being of the client as well as public health consequences on the entire society. Since accurate HIV diagnosis is a crucial component in the fight against HIV/ AIDS pandemic, it is imperative that suitable diagnostic kits are selected and the best algorithm designed for the diagnosis of HIV in the country. A couple of factors take center stage in the selection of specific tests in a country's algorithm, one of them being the test performance in the country. This performance is based on how close a test under consideration agrees 100% with the result of another test, usually referred to as the reference method or "gold standard". Other factors include: test availability in country, program needs, ease of use, type of specimen, cost, and etc. [HIV Testing Strategies and

Algorithms, Participants Manual, 2005]. The ideal algorithm used is one in which tests are highly sensitive and highly specific [HIV Testing Strategies and Algorithms, Participants Manual, 2005].

The National AIDS Control Program (NACP), Ghana, developed the serial testing algorithm, in which the First Response HIV-1-2-test kit is used as the screening test and all positive samples are confirmed with the Oraquick Advance HIV-1-2 Antibody test. Discordant results are resolved using the ELISA as a tiebreaker.

Aim

To assess the efficiency and public health implications of the NACP developed HIV testing algorithm.

Method

A systematic review on the diagnostic accuracy of the undermentioned rapid kits was conducted; First Response HIV-1-2 kit (Premier Medical Corporation Ltd., Kachigam, India) and the Oraquick Advance HIV-1-2 kit (OraSure Technologies, Bethlehem, PA, USA). Literature search strategies using a search algorithm consisting of terms for: HIV, rapid diagnostic tests, evaluation, diagnostic accuracy and Anti-HIV antibodies in various combinations with the names of these kits were used. Searches were made in Africa Journal online, Pubmed, Google scholar and some institutions in the country. Searches were also made in the websites of the ministry of health, Ghana Health service and the NACP for non-indexed studies or reports on the subject. Abstracts were screened according to standard inclusion and exclusion criteria for selection of articles or papers for the systematic review.

Selection criteria

Inclusion

Studies reporting original data from patients, irrespective of the study-design, sample size and age groups which use only blood-based specimens, conducted in any setting (laboratory or field) and in English language only with the primary purpose of evaluating the diagnostic accuracy of the aforementioned brand of rapid kits and comparison studies using a reference standard.

Reference standards considered acceptable included enzyme immunoassay, enzyme-linked immunosorbent assay, line immunoassays, microparticle enzyme immunoassay (MEIA) and PCR.

Exclusion

Articles in non-English language, studies only reporting prevalence, studies without comparison to a reference standard, comments, reports from the manufacturers and package inserts due to possible conflict of interest.

Extraction

The following were extracted from each study to generate a table: study author, year of publication, location of study, index test (the rapid test of interest), sample type, sensitivity and/ or specificity report. Specific information about the index tests which included: name of the test, country of origin, name of the manufacturer and manufacturers' test indices (sensitivity and specificity) were extracted from the package insert and study.

Results

Result of studies on evaluation of the rapid kits

A total of 28 full text articles and abstracts were examined which identified 15 studies meeting pre-defined criteria.

Table 1 result of studies on evaluation of the rapid kits in Ghana A total of 4 studies which evaluated the First Response HIV-1-2 kit and the Oraquick Advance-HIV-1-2- Antibody test was found.

Table 2 result of studies on evaluation of the rapid kits in other parts of the world A total of 10 studies, five of which evaluated the First Response HIV-1-2 kit and the remaining five, the Oraquick Advance-HIV-1-2- Antibody test was found.

Table 3 specificity of first response and oraquick using different specimen types For the First Response HIV kit, a specificity range of 82.56%-92.00% with a mean of 87.40% was obtained for evaluation studies in Ghana using serum and a range of 90.4%-98.4% with a mean of 96.10% for studies in other parts of Africa using serum. For the OraQuick Advance HIV kit, a specificity range of 99.8%-99.98% with a mean of 99.90% was obtained for evaluation

studies across the world using whole blood, a range of 94%-100 with a mean of 98.20% for studies across the world using serum/plasma and a specificity range of 98.8%-100% with a mean of 99.30% for all studies regardless of specimen type across the world excluding studies in Ghana.

Table 1. Result of studies on evaluation of the rapid kits in Ghana

Study	**Location**	**Test under evaluation**	**Sensitivity (%)**	**Specificity (%)**
Author/year	**Country**	**Type/Brand**		
Okyere, D.A. (2018)	Ghana	First Response HIV-1-2-test	99.0[1]	92.0[1]
Amoatika, D.A. (2019)	Ghana	First Response HIV-1-2-test	88.0[1]	92.0[1]
Tetteh, A.K. (2017)	Ghana	First Response HIV-1-2-test	94.21[1]	82.56[1]
Boadu, R (2016)	Ghana	First Response HIV-1-2-test	100[1]	82.86[1]
			100[2]	100[2]
Amoatika, D.A. (2019)	Ghana	OraQuick Advance HIV antibody test	98.0[1]	94.0[1]

Note: [1] Serum [2] Whole blood

Table 2. Result of studies on evaluation of the rapid kits in other parts of the world

Study	**Location**	**Test under evaluation**	**Sensitivity (%)**	**Specificity (%)**
(Author/year)	**(Country)**	**Type/brand**		
Kagulire, S.C. et al (2011)	Uganda	First Response HIV	1001	97.41
Lyamuya, E.F. et al (2009)	Tanzania	First Response HIV	1002	99.62
Bassey, O. et al (2014)	Nigeria	First Response HIV	98.91	98.41
Kosack, C.S. (2017)	Sub-Saharan Africa	First Response HIV	98.83	90.43
Dagnra, A.Y. et al (2014)	Togo	First Response HIV	991	98.11
Pai et al (2012)	Several sources	OraQuick HIV	99.682	99.912
Choi et al (2009)	Korea	OraQuick HIV	1001	98.81
Wesolonski et al. (2006)	USA	OraQuick HIV	Not reported	99.982
Eller, L.A. et al (2007)	Uganda	OraQuick HIV	1002	99.82
Loukou et al (2014)	Ivory Coast	OraQuick HIV	1001	1001

Note: 1 Serum 2 Whole blood 3 Plasma

Table 3. Specificity of first response and oraquick using different specimen types

	First response[1]	**First response[1]**	**Oraquick[2]**	**Oraquick[1, 3]**	**Oraquick[1,2,3]**
	Ghana	**Africa**	**Global**	**Global**	**Global excluding Ghana**
	92	98.4	99.91	98.8	99.91
	92	90.4	99.98	94	99.98
	82.56	97.4	99.8	100	99.8
	82.86	98.1	-	100	100
	-	-	-	-	100
	-	-	-	-	98.8
Mean	87.40%	96.10%	99.90%	98.20%	99.30%

Note: 1 Serum 2 Whole blood 3 Plasma.

Discussion

HIV counseling and testing is considered a top priority in national response to the fight against HIV/AIDS pandemic. The sensitivity and specificity of a test are crucial factors in determining the test's ability in correctly distinguishing between infected and uninfected individuals. It is important that the HIV tests used in an algorithm all have a sensitivity of at least 99% and a specificity of at least 98% [WHO 2015], in order to ensure accurate

detection of HIV-infected persons who will benefit from treatment, care and support services as well as those who are free of the infection and will need information to remain uninfected. The National AIDS Control Program (NACP) has developed a serial HIV testing algorithm which makes use of two types of rapid assays; the First Response HIV-1-2 kit and the Oraquick Advance HIV-1-2 kit. In this algorithm, the First Response HIV-1-2 test kit is used as the screening test and all reactive samples are confirmed using the OraQuick Advance HIV-1-2 rapid kit. If a sample is reactive with the First Response HIV-1-2 rapid test kit but tests negative on the OraQuick Advance HIV-1-2 rapid test kit, the discordant result is resolved using ELISA as the tie breaker.

The First Response HIV-1-2 kit is a pre-qualified WHO and FDA approved kit with a manufacturer's sensitivity of 100% and specificity of 100%. A number of post- market independent evaluations of the First Response HIV-1-2 kit have been done .This review found four studies that evaluated the First Response HIV-1-2 kit for the screening of blood for anti-HIV-1 and 2 antibodies in Ghana with sensitivity ranging from 88% to 100% and a specificity range of 82.56% - 92.0% with an average of 87.36% when serum was used as the specimen of choice [Okyere DA (2018), Tetteh AK et al (2017), Boadu R et al. (2016), Amoakita DA et al (2019)]. Studies conducted in other parts of Africa, however, reported an average specificity of 96.08% for the First Response HIV-1-2 rapid kit with serum specimens, which is significantly better than those observed in Ghana [Kosack CS et al. (2017), Kagulire SC et al (2011), Dagnra AY et al (2014), Bassey O. et al (2014)]. From the studies identified in Ghana, both the sensitivity and specificity of the First Response rapid kit varied considerably when serum specimen was used as the specimen of choice for testing. An average specificity of 87.36% was obtained in the performance assessment of the First Response rapid kit in Ghana using serum specimen, which translates into an approximate false positive rate of 13%. The implication for this is that, approximately 13% of the people who test with the First Response HIV test kit using serum specimens will obtain false positive results. In the current HIV testing algorithm for the country, all false positive results, same as true positive results from any screening exercise will have to be confirmed with the OraQuick Advance HIV-1-2 rapid test kit. With the high false positive rate of approximately 13% for the First Response HIV-1-2 kit using serum specimens, the OraQuick Advance HIV-1-2 rapid test kit, which is used as the supplemental test in this algorithm, must be highly specific to be able to differentiate between those who are truly infected and those who are uninfected. The OraQuick Advance HIV-1-2 kit is also a pre-qualified WHO and FDA approved kit with a manufacturer's sensitivity of 100% for both whole blood and plasma and specificity of 100% also for both whole blood and plasma. Only one study on post-market assessment of the OraQuick Advance HIV-1-2 kit, the supplemental assay in the current HIV testing algorithm used in Ghana, was found after extensive literature search. A sensitivity and specificity of 98% and 94% respectively, which did not meet the WHO's and FDA's minimum performance criteria for HIV diagnostic assays was reported by the investigators [Amoakita DA (2019)]. The manufacturer's specificity suitability claim has, however, been corroborated by a number of independent field evaluations in other parts of the world. Seven studies were identified with an average specificity of 99.68% [Pai et al. (2012), Choi et al. (2009), Wesolowski et al. (2006), Eller LA et al (2007), Bassey O et al(2014), Loukou et al(2014), Piwowar-Manning, EM et al (2010)], which does not come as a surprise because of differences in performances of diagnostic assays under different testing conditions. These variations in performances have been attributed to the existence of extensive genetic diversity and abnormal variants especially in Africa, concomitant infections and the underlying prevalence of exogenous and endogenous infections/substances, which is likely to vary from region to region and country to country [Kosack CS et al (2017)].Unfortunately, this review, based on the data available, though not sufficient, hasn't been able to prove the superior specificity of the OraQuick for use as a supplemental assay with fears of a patient misdiagnosed of HIV and exposed to unnecessary and potentially toxic medical treatment as reported by Amoakita et al. With the false positive rate of the First Response HIV-1-2 test kit using serum, it can be inferred that

approximately 13% of the results will likely be discordant requiring the use of a tie breaker which is more expensive and unavailable in most of the remote laboratories. This will definitely delay the test results and negate benefits which might have been made with an instant confirmatory result. Though only few studies used whole blood as specimens for evaluation in the reports obtained, it was noted that for both the First Response HIV rapid test kits and the OraQuick Advance HIV rapid test kits, the specificity was better when whole blood was used as the specimen of choice. An average specificity of 99.9% for whole blood as against 98.2% for serum/plasma was obtained for the OraQuick Advance HIV-1-2 antibody test and with the First Response HIV-1-2 test kit, when whole blood was used, the specificity jumped from 82.36% to 100% [Boadu et al (2016]. This will bring down significantly, the number of false positive results and the unnecessary confirmatory tests that have to be performed, saving cost in the process if the specimen of choice is restricted to whole blood. This finding agrees with a study by Lyamuya et al, who reported a specificity of 99.9% when whole blood was used as against 99% for serum [Boadu et al (2016]. Generally, serum specimens are known to contain various antibodies that may bind to reaction sites meant for target antibodies [Abokyi LV (2014)] and this may explain the reduced specificity when serum specimens are used as specimen for testing on some rapid diagnostic test kits. Two reports from this review recorded significant false negative rates averaging 8.9% with the First Response HIV-1-2 test kit in Ghana [Tetteh AK et al (2017) and Amoakita DA et al (2019)]. The eventual consequences of false negative results are very significant. False negative results are a threat to both public health prevention strategies and wellbeing of the individuals since it will prevent infected persons from enrolling in treatment, care and support programs as well as taking the necessary precautions to prevent the transmission of HIV.

Conclusion and recommendations

From the discussion, the current testing algorithm in Ghana may not be cost effective and efficient in screening and diagnosing HIV infections in the face of deficiencies in performance observed with the rapid kits especially when serum specimens are used. The significant false negative rate reported by two investigators in this review makes it worrying for the First Response to be used as a screening test in a serial testing algorithm. The superior specificity of the Oraquick Advance HIV-1-2 kit could also not be proved with fears of misclassification of uninfected individuals reported. A change to parallel testing algorithm which tests all specimens with two rapid tests that are highly sensitive and specific and resolve discordant results by retesting with a third tie breaker test in the near future, especially for pregnant women and blood donors is strongly recommended. Post market assessment must also be strengthened and validated algorithms reviewed at specified periods to ensure the tests employed perform according to specifications.

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