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HCV Diagnosis in Ghana – Limitations and Public Health Implications

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Abstract

Hepatitis C infections have become public health concern globally and in Ghana, 1 in14 cases of cirrhosis is caused by HCV. Diagnosis and treatment remain crucial in the control and prevention of this epidemic. The purpose of this study was to examine the types of rapid assays and testing algorithms used for the screening and diagnosis of HCV in Ghana.

Structured questionnaires were sent to selected public and private laboratories across the country to elicit responses on the types of rapid assays and testing algorithms used for the screening and diagnosis of HCV. Searches in online journals, credible websites and institutions were done to access evaluation reports on the rapid kits in Ghana to determine their suitability for use and the efficiency of the algorithms. Seventeen different rapid kits were found to be in use in the facilities sampled. Only 2 out of the 17 were WHO prequalified. DiaSpot, the most widely used test kit was neither WHO pre-qualified nor FDA approved. Very limited information on evaluations was found in Ghana. All the facilities sampled use a single assay testing strategy.

This study revealed that the reliability of the rapid kits used in the testing algorithms in Ghana cannot be guaranteed and thus may not be efficient for screening and diagnoses of HCV infections in Ghana. There was also no public or private facility sampled which does Nucleic Acid Testing, making the definitive diagnosis of HCV very difficult.

Keywords: *Rapid assays, Suitability, HCV, NAT.*

Introduction

Hepatitis C virus (HCV) is a major global health burden accounting for around 170 million chronic infections worldwide [Dustin LB et al (2016)]. Several developments have taken place since the discovery of the HCV which includes improved diagnostic tools and approval of newer therapies, changing the frontiers of HCV management [Tachi K (2018)]. Because of the socioeconomic burden this pandemic pose, many nations now consider HCV infection a priority and are putting measures in place to curb the further spread of the infection. The prevalence of HCV infection in Ghana is estimated at 3% [Ofori-Asenso et al (2016)] but the true prevalence is mostly likely to be higher than this since there is no national screening policy and most of the prevalence studies involved blood donors and pregnant women, who are within the low risk population. According to Blankson et al, 1 in14 cases of cirrhosis is caused by HCV in Ghana.

Because the infection is clinically silent in majority of carriers until late, the true prevalence and the burden it imposes on the Ghanaian health care system is likely to remain unknown unless a comprehensive national screening policy is implemented [Tachi K (2018)]. The national guidelines for prevention care and treatment of viral hepatitis in Ghana, which was launched in 2017, recommends the use of WHO Pre-qualified kits for screening.

Because no HCV vaccine exists, testing and treatment of infected individuals is the gateway to controlling this pandemic and this can only be achieved if the ideal testing algorithm is used for screening and diagnosis. An ideal algorithm is one in which the tests used are highly sensitive and specific.

Aim

The aim of this study was to examine the types of rapid assays and testing algorithms used

for the screening and diagnosis of HCV in Ghana.

Method

This was a cross sectional study design and was conducted across selected public and private laboratories in Ghana. A total of 426 facilities, compromising of 226 public and 200 private facilities across the country were sampled for this study. Information on types of rapid assays used for HCV screening as well as the testing algorithms used was collected using a well-structured questionnaire. The questionnaires were sent to all the facilities across the country and were completed by certified laboratory scientists of varying ranks within those facilities. The relevant responses or information elicited by the questionnaires were categorized and analyzed.

A systematic review on the diagnostic accuracy of the rapid kits in use was conducted.

Literature search strategies using a search algorithm consisting of terms for: HCV, Anti-HCV, rapid diagnostic tests, evaluation and diagnostic accuracy, in various combinations with the names of the 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 and Ghana Health service for non-indexed studies or reports on the subject. Researchers who had published papers on related subjects were also contacted for extra information.

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, 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.

Result

Diversity of rapid kits for HCV

A total of 17 different rapid assays were found to be in use with the DiaSpot (DiaSpot Rapid Diagnosis, Indonesia) being the prevalent type. 83 facilities representing 22.2% use the DiaSpot.

The Advanced Quality (InTec Products Inc, China) was the prevalent type among the public facilities whilst the DiaSpot (DiaSpot Rapid Diagnosis, Indonesia) was the prevalent type among the private facilities. Details are outlined in the table below. Only 374 out of the 426 facilities performed anti-HCV antibody screening.

Results of studies on the HCV rapid kits in use

A total of 39 full text articles and abstracts were examined which identified 22 studies meeting pre-defined criteria. One was in Ghana and the remaining 21 in Africa and other parts of the world.

Table 1. Diversity of rapid kits for HCV among public and private facilities

	Number of Facilities			
	HCV			
Name of Kit	**Public**	**Private**	**Total**	**%**
Wondfo	11	15	26	6.95
Micropoint	15	16	31	8.29
Core tests	9	3	12	3.21
Solid	0	0	0	0
Two dot	0	0	0	0
Diaspot	40	43	83	22.19
Greenlife	0	0	0	0
Juschek	10	4	14	3.74
Acon	8	33	41	10.96
Advance quality	49	32	81	21.66
Right sign	16	20	36	9.63
Hightop	4	5	9	2.41
Aria	0	8	8	2.14
Sd bioline	0	5	5	1.34
Accu-tell	9	3	12	3.21
Lumiquick	0	2	2	0.53
Biosure	0	2	2	0.53
Globatest	0	1	1	0.27
Cortez	0	2	2	0.53
Oscar	7	2	9	2.41
Total	**178**	**196**	**374**	**100**

Table 2. Results of studies on the HCV rapid kits in use in Ghana

Study	**Location**	**Test under evaluation**	**Sensitivity (%)**	**Specificity (%)**
Author/Year	**Country**	**Type/Brand**		
Dogbe EE et al (unpublished)	Ghana	Acon Anti-HCV	25%	-

Table 3. Results of studies on the HCV rapid kits in use in other parts of the world

Study	**Location**	**Test under evaluation**	**Sensitivity**	**Specificity**
(Author/Year)	**(Country)**	**Type/Brand**	**(%)**	**(%)**
Mane et al. (2019)	India	Advanced Quality HCV	96.3	100
Bigwan et al. (2014)	Nigeria	Wondfo HCV	75	99
Waheed et al. (2017)	Pakistan	Advanced Quality HCV	83.33	100
Jargalsaikhan et al. (2016)	Mongolia	Wondfo HCV	100	96.77
Jargalsaikhan et al. (2016)	Mongolia	Advanced Quality HCV	100	97.78
Hayder, I. et al (2012)	Pakistan	Acon HCV	93	93
O'Connell. et al (2012)		CORE HCV	34.5	
Al-Tahish, G. et al (2013)	Egypt	ACON HCV	97	77
WHO (2001)	Asia/Africa/Europe / Latin America	InTec HCV	97.1	96.3

Stokx, J. et al (2011)	Mozambique	SD Bioline HCV	100	99.1
Mane, A. et al (2019)	India	SD Bioline HCV	99.4	100
International Red Cross	Germany	Advanced HCV	99.7	99.8
INSERM	France	Advanced HCV	99	99
ONOM Foundation	Mongolia	Advanced HCV	100	97.83
Hepatitis Network	Iran	Advanced HCV	100	100
Maity, S. et al (2012)	India	SD Bioline HCV	100	100
Jargalsaikhan et al. (2016)	Mongolia	SD Bioline HCV	96.67	97.78
Laperche, S. et al (2013)	17 African countries	Accu-Tell HCV	100	100
Laperche, S. et al (2013)	17 African countries	SD Bioline HCV	72.2	96.4
Yuen et al (2001)	China	Advanced HCV	97.1	96.3
Torane & Shastri (2008)	India	SD Bioline HCV	96.9	100

Discussion

Out of the 426 facilities sampled, 374 were equipped to perform anti-HCV antibody screening. A total of seventeen different rapid kits were found to be in use by the public and private facilities. Of the seventeen, the DiaSpot rapid kit, manufactured by DiaSpot Rapid Diagnosis, Indonesia, was the most widely used (19.5% of the respondents use DiaSpot Anti-HCV) and this kit is neither WHO pre-qualified nor approved by FDA Ghana for routine use.

This study revealed very little information on the suitability of rapid kits for Anti-HCV for routine use in Ghana. The only available report of independent evaluation of HCV rapid kits produced as high as 75% mean false negative rate for the Acon Anti-HCV rapid kit which was used for screening in some hospital-based blood bank facilities in Ghana [Dogbe EE et al (unpublished)].

Reports of several studies from other parts of the world have identified significant differences in performance of some of these Rapid Diagnostic Tests under various testing conditions and in different geographical settings. For example, a sensitivity range of 83.33% to 97.1% and specificity of 96.3% to 100% respectively were recorded for the Advanced Quality kits (InTec) when these kits were evaluated in India, Pakistan, China and Mongolia [Mane et al. (2019), Waheed et al. (2017) and Jargalsaikhan et al. (2016), Yuen et al (2001)], a sensitivity and specificity range of 99% to 100% and 99% to 100% respectively, were recorded when these same kits were evaluated in France and Iran (INSERM and Hepatitis network), sensitivity and specificity of 75.0% and 99%, and 100% and 96.77 respectively, were recorded for the Wondfo Anti-HCV kits when they were evaluated in Nigeria and Mongolia respectively [Bigwan et al. (2014), Jargalsaikhan et al. (2016)]. The Acon also recorded a sensitivity and specificity of 97% and 77% and 93% and 93% when they were evaluated in Egypt and Pakistan respectively [Al-Tahish G. et al (2013), Hayder I. et al (2012)]. These results pattern revealed significant variations in sensitivity of the test kits in comparison with the values quoted by the manufacturer with the exception of the Advanced Quality kit which was evaluated in France and Iran.

Factors attributed to the variations in performances of some rapid assays in evaluation studies include the use of samples containing low HCV antibody levels [Laperche S. (2013)], weak reactions of antibodies and use of rapid diagnostic test kits in real life conditions rather than ideal conditions seen in reference laboratories. Other factors attributed to the suboptimal sensitivities of RDTs include inadequate coating of the antigens, the nature of the antigens used, and genetic heterogeneity of

the virus, e.t.c. [Torane and Shastri (2008). For these reasons, the Drug Control General of India (DCGI), the national regulatory authority, for example has laid acceptance criteria (sensitivity > 99% and specificity of at least 98%) to which all Anti-HCV rapid kits must conform to before they are approved for use in India (Mane A et al (2019) and it is imperative that rapid kits imported and marketed for use on the Ghanaian market must be subjected to such stringent national regulatory checks in order to protect the health of the public.

The responses gathered from this study showed that all the facilities sampled use a single-test algorithm. Prevalence of HCV in Ghana is 3.0% [Ofori-Asenso et al (2016)], which is considered high and therefore a single-test algorithm would have been suitable as long as the rapid kits in use are highly sensitive and specific. With the few reports of evaluation of Hepatitis C rapid kits in Ghana and the poor performance of these same kits in other parts of Africa and the world coupled with the lack of information on the suitability of most of the rapid kits available for use on the Ghanaian market, it is likely that the current kits being used by these laboratories may lack the minimum requirements to be included in any testing algorithm in Ghana and with the need to scale up screening, having poor sensitivity and thus potentially missing HCV-infected individuals would have serious drawbacks for the program with its attending public health challenges.

Definitive diagnosis of chronic hepatitis C viral infection requires both a positive HCV antibody test and a positive HCV RNA test. The national guidelines for prevention, care and treatment of viral hepatitis in Ghana, which was launched in 2017 recommends the use of WHO Pre-qualified kits for screening and diagnosis of Hepatitis C but of interest is that, this study has revealed that apart from the SD Bioline and the Advanced Quality HCV rapid tests, all of the rapid kits being used for screening of Hepatitis C in both the public and private facilities, including the most widely used DiaSpot, are neither WHO pre-qualified nor approved by FDA Ghana.

Whiles most of the facilities sampled have the capacity to perform the screening of anti-HCV antibody test, none in the country is equipped to perform HCV RNA or viral load and genotype testing. Samples for these tests have to be sent abroad at minimum turnaround time of one week and a cost beyond the means of most Ghanaians, making the diagnosis and treatment of HCV infection very difficult.

Conclusion

In conclusion, the performance of the rapid kits being used for Anti-HCV screening cannot be guaranteed and thus may not be suitable to be included in any screening algorithm in Ghana.

Recommendations

1. A national algorithm which makes use of sensitive and specific tests must be developed.
2. The Food and Drugs Authority must regulate the influx of Anti-HCV rapid kits and ensure that only kits evaluated and approved for use in Ghana are allowed to be imported and sold on the Ghanaian market
3. The FDA should also conduct random post-market assessments of the test kits to ensure that the required performance characteristics are maintained at all times.

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