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CARE START™ MALARIA PAN (PLDH) AG RDT QUALITY ASSESSMENT IN SELECTED HEALTH FACILITIES OF AREZA SUB ZONE, ERITREA

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ABSTRACT

Background: In Eritrea malaria is still remains a public health concern despite the drastic decline in morbidity and mortality. Malaria RDT is highly used as a diagnostic tool in health stations and community health agents, while blood film or microscopy used from health center and above in Eritrea. **Objective:** The study aimed to explore the quality of Care Start™ Malaria PAN (PLDH) Ag RDT which is used to diagnose malaria in health stations and community health agents in selected health facilities of Areza sub zone. **Methods:** This study was carried out as a cross-sectional laboratory survey during the period (July - September 2020). The study was carried out in 3 selected health facilities of Areza sub zone, southern region, Eritrea, which were selected randomly. The study tested 139 RDT's. Health facilities having microscopy cross checked RDT so as to know the quality and accuracy of RDT. A systematic random sampling was used for selecting the RDT. After collection of the data, the variables (responses) were coded and entered into SPSS software version 23 and cleaned. Descriptive statistics was used to compare results among the study groups using frequency distribution count and percentages. **Results:** At control line 46% becomes very bright and 48.5% at 'T' line, where as 54% of control line and 51.5% becomes faint. 4.7% of the RDT result becomes false negative result (in Blood film, result positive whereas RDT, result negative). 3.5 % invalid result has been obtained from RDT test assessment. Some RDT appear faint in test line after 20 minute but was confirmed as Negative result by Blood film. **Conclusion:** As the time is extended, the RDT result changed and this leads to wrong reading result. Therefore it is very difficult to decide whether the patients to be treated or not. This RDT is difficult for CHA to interpret the result, as a result there was more complain from CHA and other Health facility having RDT.

KEYWORDS

Malaria, RDT, Assessment and Health facilities.

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INTRODUCTION

Mosquito-borne diseases (MBDs) threaten the lives and livelihoods of millions of people worldwide[1]. According to WHO (2020), the estimated number of malaria deaths stood at 405,000 in 2018 alone.

Children less than five years and pregnant mothers are the most vulnerable groups affecting by malaria; in 2018, they accounted for 67% (272,000) of all malaria deaths globally[2]. The WHO African region carries a disproportionately high share of the global malaria burden. According to WHO, in 2018 the region was home to 93% of malaria cases and 94% of malaria deaths. WHO estimates that there are approximately 3.2 billion people at risk of contracting malaria[2] Malaria exerts excessive continuous huge public health burden in most of developing poor countries[3,4]. Currently, the disease burden is estimated at 45.6 million DALYs (disability-adjusted life years)[5]. Hence, it has been identified as a key contributor to weak economic growth and investment in Africa, because it experiences the most intense malaria transmission in the world[6]. Likewise, malaria causes high morbidity in Eritrea especially in Gash Barka region, and it is endemic in other three zones of the country *Vis*. Northern red sea (NRS), Debub and Anseba and 70% of the estimated population resides in malaria endemic areas[7]. Malaria is caused by five species of parasite that affect humans, and all of these species belong to the genus *Plasmodium (p): P. falciparum, P. vivax, P. ovale, P.malariae* and *P. knowlesi*. Of these, *P. falciparum* and *P. vivax* are the most important. Malaria due to *P. falciparum* is the most deadly form, and it predominates in Africa[8]. *P. vivax* has a wider distribution than *P. falciparum*, because it is able to develop in the *Anopheles* mosquito vector at lower temperatures, and to survive at higher altitudes and in cooler climates[8]. Malaria is transmitted by a bite of infected female *An.* mosquitoes. Worldwide, there are approximately 48 species which is considered as vectors of human malaria[9].

The burden of malaria in Eritrea is declining from year to year. Evidenced by 89% reduction in malaria incidence from 157 cases/1000 population at risk in 1998 to 17 cases /1000 population in 2016. At the same time, there was a 98% reduction in malaria specific deaths from 0.198 deaths/1000 population to 0.004 deaths/1000 population[10]. The latest Malaria indicator survey in 2012 has found the prevalence as 1.1% in the general population[11]. This improvement has attached Eritrea with the description of a country achieving 'the biggest breakthrough in malaria mortality prevention in history'[12]. Some of the main core values for attaining this reduction was effective case detection and management in accordance to the WHO guideline. Where hierarchical management of cases according to severity has been employed and supplies such as Antimalarial Combination Therapy's (ACT's) and Rapid Diagnostic Tests (RDTs) were expanded as low as to the community level. For the detection of malaria, Hospitals and Health Centres are equipped with microscopy, Heath Stations and Community Health Agents use RDT's. Artesunate + Amoidiaquine combination is the recommended treatment from the five ACTs. Moreover, vector control strategies including, distribution of LLINs, spraying of household indoors with Insecticidal spray and larval source management, in combination with efficient epidemic preparedness and response and program management tools were implemented[13].

RDTs are immunochromatographic tests based on the detection of specific parasite antigen. The parasite antigen are HRP2, Pldh and aldose. Some RDTs detect more than one parasite protein and are called pan-specific. RDTs are sensitive in detecting low parasitemia. RDTs can't be used to determine the density of parasite. RDTs can't be used for follow up. It's simple to use. RDTs are not 100% sensitive.

RDT is used where there is no microscopic setting. Microscopy is used in laboratory setting with microscope and accepted gold standard if competent microscopist is in place. Malaria test done in Areza sub zone from 2017-2020 were 41,909, 14.6% were tested by blood film or microscopy and majority of the test, 85.4% were conducted by RDT. Therefore, since the majority of the test was conducted by RDT, this study aimed to explore the quality of Care Start™ Malaria PAN (PLDH) Ag RDT in selected health facilities of Areza sub zone.

MATERIAL AND METHODS

Study design

This study was carried out as a cross-sectional laboratory survey during the period (July – September 2020).

Study area

The study was carried out in 3 selected health facilities of Areza sub zone, southern region, Eritrea. Areza Sub Zone is one of the 12 Sub Zones of Southern region, which is located 42km to west away from Mendefera. There are 7 health facilities in the sub zone. The selected health facilities were Zibandebri health station; Maidma health center and Areza health center. Zibandebri health station; is a health facility found 32km away from Areza health center south ward. Its altitude is 2,140 meters from sea level. Maidma health station; is a health facility found 18km away from Areza health center west ward. Its altitude is 1,543meters from sea level. Areza health center is a health facility found 42km away from Mendefera west ward.

Study population

Care Start™ Malaria PAN (PLDH) Ag RDT was the study population.

Sample size and Sampling Method

The study tested 139 RDT's. A systematic random sampling was used for selecting the RDT. The 3 health facilities were selected randomly.

Data Collection Techniques and Tools

Using RDT, patients having malaria sign and symptoms were tested for malaria. Since Areza and Maidma health center had microscopy, RDT was cross checked by microscopy to confirm its accuracy and quality. While, in zibandebri health station, it was tested only by RDT. This was not cross checked by microscopy, since it wasn't available in the health station, but we observed the RDT, whether the control and test line is available and the lines brightness, is it clear to decide or not.

Care Start™ Malaria PAN (PLDH) Ag RDT contains a membrane strip, which is pre-coated with monoclonal antibody as a single line across the strip. The monoclonal antibody is specific to PLDH of the plasmodium species (*P.Falciparum, P. Vivax, P. Ovale and P. Malariae*). The conjugated pad is dispensed with antibody absorbed on gold particles.

For the rapid qualitative detection of malaria PLDH (plasmodium lactate dehydrogenase) in human whole blood serves as an aid in the diagnosis of malaria infection of *P. Falciparum, P. Vivax, P. Ovale, P. Malariae*.

Test principle

Care Start™ malaria pf/pv (HRP-2/pLDH) Ag combo RDT is designed to detect HRP-2 Ag for PF and pLDH Ag for Pv and PF.

But since the HRP-2 Ag has been deleted in our country second RDT is needed to detect PF which is CareStart ™ malaria PAN (pLDH) Ag RDT.

CareStart ™ malaria PAN (pLDH) Ag RDT is designed to detect the pLDH Ag of either plasmodium malaria, plasmodium ovale, plasmodium vivax or plasmodium falciparum.

Test procedure

Collect blood from the pricked finger or test tube using inverted cup pipette and place the sample in the 'S' part of test cassette.

Then add 2 drops of buffer in to the well-marked 'A'.

Wait 20 minutes to know the result.

How to test and report

First test the patient with Care Start™ malaria PAN (pLDH) Ag RDT, then see the result.

If it is negative finish it, as negative.

If it is positive, continue testing with malaria pf/pv (HRP-2/pLDH) Ag combo RDT

Data analysis method

After collection of the data, the variables (responses) were coded and entered into SPSS software version 23 and cleaned. Descriptive statistics was used to compare results among the study groups using frequency distribution count and percentages.

Ethical Clearance

For ensuring the privacy of respondents and preventing violation of human rights, the proposal was approved at the Ministry of Health Scientific and Research Ethical Committee. After securing permission from the MOH, letter of support was sent to MOH Areza sub zone for allowing data collection. Informed consent was obtained from each respondent after a thorough explanation of the aim and potential benefits of participating in the study

was given, and written consent was signed by the respondents.

RESULTS AND DISCUSSION

Special findings

In blaze, at control line 46% becomes very bright and 48.5% at 'T' line.

In Faint, at control line 51% becomes faint and 30.4% at 'T' line.

In efface, at control line 2.8% becomes very faint and 16.2% at T line.

4.7% of the RDT result becomes false negative result (in Bf, result positive whereas RDT, result negative).

3.5% invalid result has been obtained from RDT test assessment.

80% of the control and test line result were Read at 20 min, 18.7% from 20-60 min and 1.3% were Read after 1hr.

Some RDT appear faint in test line after 20 minute but was confirmed as Negative result by Blood film.

Not confidently to report whether positive or negative due to hesitated brightness.

Discussion

Malaria diagnostic should be assured its quality so as to continuously and systematically improve the efficiency, cost-effectiveness and accuracy of results. It is essential that Quality assurance ensures: the clinical team have full confidence in the lab results, the diagnostic results are of benefit to the patient and community, the competency of the lab personal is approved and the performance of the lab is approved. These demands can only be met through a commitment to QA program that ensures the lab services are: stuffed by competent and motivated stuff, supported by both effective training and supervision, a logistics system that provides an adequate and continual supply of quality reagents and essential equipment that are maintained in appropriate working order. QA is not a goal to be reached, but an ongoing process that ensures the maintenance and quality of a job (malaria microscopy and RDT).

Zibandebri H/S result

Control result

Out of 46 RDT tests 24 RDTs result at 'C' line and are very visible to read them (52.2%) and the remaining 22 RDTs result at 'C' line becomes faint (somehow difficult to read it) meaning 47.8% of the tests . Therefore, these RDT results make health workers and CHAs to give wrong decision at a reading time. This leads them not to report those who had malaria due to its faintness or effaceness.

Test line result

Out of 32 positive tests only 19 positive tests becomes very *bright* in 'T*' line* which is 59.3% , 08 positive RDTs tested become *faint* in 'T*' line which is* 25% of the total tests and the remaining 05 positive RDTs result become very difficult to read (efface) which comprises 15.7%. All the fainted and effaced 13 cases resembles to negative. This is the problem commonly seen in our sub zone.

Reading Time Result

Out of 46 RDT tests 22 RDT tests were read at 20 minutes (47.8%), 22 were read from 21-60 minutes (47.8%) and 2 RDT test were read after 1hour (4.3%). The instruction of RDT leaflet informs, after waiting 20 minutes, we have to see the result. But 52.8% of the result took more than 20 minutes.

Maidma Health center result

Control result

Out of 40 RDT tests 11 RDTs result at 'C' line and are very visible to read them (27.5%) and the remaining 27 RDTs result at 'C' line becomes faint (somehow difficult to read it) meaning 67.5% of the tests. 2 RDT results becomes very faint (5%).

Test line result

Out of 30 positive tests only 15 positive tests becomes very *bright* in 'T*' line* which is 50%, 8 positive RDTs tested become *faint* in 'T*' line* which is 26.6% of the total tests and the remaining 07 positive RDTs result become very difficult to read (efface) which comprises 23.4%. All the fainted and effaced15 cases resembles to negative.

Areza health center result

Control result

Out of 53 RDT tests 29 RDTs result at 'C' line becomes very visible to read it (54.7%) and the remaining 22 RDT result at 'C' line becomes faint (somehow difficult to read it) meaning 41.5% of the tests and 2 RDTs result become very efface (3.8%).

Test line result

Out of 43 positive tests only 17 positive tests become very *bright* in 'T*' line* which is 39.5% , 16 positive RDT tested become *faint* in 'T*' line which is* 37.2% of the total tests and 5 positive RDT result becomes very difficult to read (efface) which comprises 11.6%. The remaining 5 RDT result become negative despite the Blood film is positive. All the fainted and effaced 13 cases resembles to negative.

Reading Time Result

Out of 53 RDT tests 49 RDT tests were read at 20 minutes (92.4%) and 4were read from 21-60 minutes (7.6%).

Table No.1: Malaria cases in Areza sub zone from 2017-2020

S.No	Years	Health facility		CHA		Total		Malaria Test positivity rate
		Test	Positive	Test	Positive	Test	Positive	
1	2017	5170	1564	4830	1488	10000	3052	30.5%
2	2018	5434	949	4965	1000	10399	1949	18.7%
3	2019	5989	1239	4969	1219	10958	2458	22.4%
4	2020	5201	1036	5351	1070	10552	2106	20%

Table No.2: Result interpretation

S.No	PAN (pLDH) Ag RDT		Malaria pf/pv (HRP-2/pLDH) Ag combo RDT			Result/Report
	'C' line	'T' line	'CON' line	'PF' line	'PV' line	
1	positive	negative	-	-	-	Negative
2	positive	positive	positive	negative	Negative	PF
3	positive	positive	positive	positive	Negative	PF
4	positive	positive	positive	negative	Positive	PV
5	positive	positive	positive	positive	Positive	Mixed
6	negative	invalid	negative	invalid	invalid	Invalid

Table No.3: Total BF and RDT test done in the health facilities

S.No	Health Facility	Total BF Done	Total RDT Done	Positive	Negative	False negative
1	Zbandebri H/S	0	46	32	14	0
2	Maidma H/S	40	40	30	10	0
3	Areza H/C	53	53	43BF and 38 RDT	10	05
4	Total	93	139	105	34	05

Table No.4: Comparing the brightness of control and test line in selected health facilities

S.No	Health Facility	Blood Film Result	RDT brightness of control and test line Result											
			blaze		Faint		efface		Negative		Reading Time			False Negative
			C	T	C	T	C	T	C	T	20 min	21-60 min	>1 hr	
1	Zibandebri H/S	0	24	19	22	08	0	05	14	0	22	22	02	0
2	Maidma H/S	40	11	15	27	8	2	7	0	0	40	0	0	0
3	Areza H/C	53	29	17	22	16	2	5	0*	5*	49	4	0	05
	Total	93	64	51	71	32	04	17	0	05	111	26	2	05

* indicates invalid

Number of RDT test done by Areza = 53 (38 positive, 10 negative and 05 invalid), Zbandebri =46 (32 positive, 14 negative) and Maidma H/s 30/40 Positive and 10/40 Negative.

CONCLUSION

As the time is extended, the RDT result changed and this leads to wrong reading result. So the cases become very difficult to decide whether the patients to be treated or not.

This RDT is difficult for CHA to interpret the result, as a result there was more complain from CHA and other Health facility having RDT.

According to RDT's leaflet instruction, it detected 100% of the samples at low density (200p/ul) and high density (20,000p/ul). It has no false positive results. But according to this study, 4.7% of the RDT result becomes false negative (in Blood film, result positive whereas RDT, result negative).

According to RDT's leaflet instruction, the brightness of the strand at the reading pool of the RDT depends on parasite count, meaning if the parasite count is low < 200 parasite, the brightness of the strand becomes faint. But according to this study the brightness of the strand at the reading pool of the RDT does not depend on parasite count; it depends on the onset of signs and symptoms. In some RDT with low parasite count, the brightness of the strand becomes blaze where as in some RDT with high parasite count, the brightness of the strand becomes faint or vice versa. So, the result of brightness becomes inconsistent.

The instruction of RDT leaflet informs, we have to see the result at 20 minutes. If it took more than 20 minutes, don't read the result. But according to the study, 20% of the result took more than 20 minutes. The study finding was not consistent with the company's leaflet instruction. Moreover, we treat the patients based on the company's instruction. In addition to this, the company informs after 20 minutes, the result may be false result, but in this finding 2 RDT give its result after 20 minutes and becomes positive for malaria and crosschecked by microscopy and the finding was positive.

RECOMMENDATION

As Care Start™ Malaria PAN (PLDH) Ag RDT causes uncertain results this RDT should be changed.

If possible RDT for screening and species identification should be on the same strip not to make confusion for CHA.

As the brightness of the strand at the reading pool of the RDT is not clear; RDTs that are more bright and clear should be provided.

As majority of the malaria cases were screened by RDT, qualified and sophisticated RDT should be provided.

The zonal malaria control program and laboratory department should introduce QC system for RDT. Based on this system every laboratory site should be responsible for checking the quality of RDTs at least quarterly with one positive and one negative samples in their site before distributing the RDTs.

LIMITATIONS OF CARESTART™ MALARIA PAN (PLDH) AG RDT

The positive result with faint tested line or a false negative is possible due to a low parasite density.

The test may still produce a positive result after successful anti-malarial treatment. Therefore, its use is not recommended for monitoring a response to anti-malarial treatment.

The test may produce a false positive result for a patient with acute schistosomiasis or a high level of rheumatoid factor.

ABBREVIATIONS

Ag: Antigen; BF: Blood Film; CHA: Community Health Agents; MOH: Ministry of Health; PF: Plasmodium Falciparum; PV: Plasmodium Vivax; QA: Quality Assurance; QC: Quality Control; RDT: Rapid Diagnostic Test; SPSS: Statistical Package for Social Sciences; WHO: World Health Organization.

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CONSENT FOR PUBLICATION

This manuscript has not been published elsewhere and is not under consideration by another journal. All authors have approved the final manuscript and agreed for its publication.

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CONFLICT OF INTEREST
None declared.

AUTHORS' CONTRIBUTIONS
All authors participated in all phases of the study including topic selection, design, data collection, data analysis and interpretation.

AVAILABILITY OF DATA AND MATERIALS
The complete data set supporting the conclusions of this article is available from the corresponding author and can be accessed up on reasonable request.

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