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Rapid Diagnostic of Malaria in Pregnant Women at their First Antenatal Care Contact within Nanoro Health District, Burkina Faso

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Abstract

Introduction: Pregnancy raises specific challenges for malaria diagnosis because of the parasite sequestration in the placenta, resulting into low parasitaemia in peripheral blood. This study aimed at assessing the performance of the ultrasensitive rapid diagnostic test (US-RDT) Alere™ Malaria Ag Pf for the detection of Plasmodium falciparum in pregnant women.

Methodology: We conducted a cross-sectional study over a four-month period from December 2020 to March 2021. This study involved pregnant women from 04 health facilities within Nanoro health district. Thick drop/blood smear, SD Bioline Malaria Ag Pf RDT-conventional, US-RDT Alere TM and qualitative PCR were performed. Performance indicators such as sensitivity; specificity; Negative Predictive Value (NPV); Positive Predictive Value (PPV) and level of concordance (kappa) were calculated for comparison. PCR was the reference test.

Results: Malaria prevalence with US-RDT, with co-RDT and PCR was respectively estimated at 45%, 45.5% and 47.4%. The prevalence of asymptomatic malaria was 34.9% with PCR as the reference test. Compared with PCR, the sensitivity of US-RDT, co-RDT and blood smear to detect infection in peripheral samples was respectively 82.3%, 75.8% and 56.6%. Sensitivity for detecting malaria in asymptomatic women was higher with US-RDT. As a whole, the specificity of the thick blood smears was better than that of US-RDT and co-RDT. The PPV and NPV of the Alere US-RDT were 86.7% and 84.8%. Concordance of results between US-RDT and PCR was good.

Conclusion: Although further studies are still needed to guide recommendations on the use of the US-RDT for malaria cases management during pregnancy, this study shows the potential value of this examination for diagnosing asymptomatic malaria during pregnancy.

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Introduction

The World Health Organization (WHO) recommends intermittent preventive treatment during pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP) in order to curb the harmful effects of malaria during pregnancy, However, several studies have also demonstrated a decrease in parasite sensitivity to SP which compromises IPTp efficiency with this drug. In West Africa, the prevalence of P. falciparum resistance to SP in pregnant women is increasing and ranges from 5 to 85% [1,2,3].

Malaria is traditionally diagnosed through a microscopic examination of blood smears. In pregnant women, Plasmodium can sequester and accumulate in the placenta which results into low parasitaemia, limiting the performance of microscopy [4,5]. The ultrasensitive rapid diagnostic test (US-RDT) Alere™ Malaria Ag Pf has been developed [6] to overcome the inability to detect low-parasitemia infections with normal RDTs. Based on recent studies, using blood samples from asymptomatic individuals has shown a better sensitivity of US-RDT compared with conventional RDT (co-RDT) in Uganda (respectively 84% vs. 62%) [6].

In Burkina Faso, few studies have evaluated the performance of the US-RDT Alere™ in pregnant women. From the above mentioned, this new US-RDT could become an optimal tool to detect asymptomatic malaria cases in pregnant women in Burkina Faso.

This study evaluated the diagnostic performance of the RDT Alere™ in pregnant women at their first contact for antenatal care within Nanoro Health District (DSN).

Materials and Methods

This study has used data collected as part of a larger study called PAMAVIT (Malaria, Viral Diseases and Toxoplasmosis) conducted by Nanoro Clinical Research Unit (URCN).

This was a descriptive cross-sectional study conducted among pregnant women at their first contact for antenatal follow-up within Nanoro Health District (DSN) from December 2020 to March 2021.

It involved all pregnant women with or without any clinical signs suggestive of malaria and coming to one of the four selected health facilities within Nanoro health district for their first antenatal care during the study period.

Considering the lack of available data on malaria infection prevalence in early pregnancy, we assumed a prevalence of 40% in order to calculate the sample size as follows: n= required sample size; Z= standard deviation at 95%, confidence interval =1.96; p= proportion of pregnant women with malaria; d= margin of error that can be tolerated, 5% (0.05); 1-p = proportion of the population without malaria.

n= (1,96)2. 0,4 (0,6) / (0,05)2 = 3,84 x 0,24/0,0025= 369

Considering a non-response rate of 5%, our sample size was estimated at 390 pregnant women.

Four health facilities were involved in the study namely: Nanoro, Kindi, Soaw and Pella. These health facilities were selected based on their geographical location (chief towns of rural communes) and the size of the population within the study area.

The sample selection was in two steps:

- The first step consisted in stratifying our sample according to the four health centers which corresponds to 98 pregnant women in each concerned maternity department.

- The second step involved a simple random sampling made to select pregnant women during their first antenatal follow-up contact (ANC) inside each maternity department.

The variable of interest was the performance of the ultrasensitive rapid diagnostic test Alere™. This is a composite indicator whose estimation takes into account other indicators.

In our study, we compared US-RDT successively with parasite microscopy and conventional RDT, using PCR as the reference test. The independent variables were the women's socio-demographic, clinical and paraclinical data.

Data were collected through a literature review of available records. PAMAVIT database was used as a data source. Data were cleaned before use. Data collection for PAMAVIT study was carried out on each study site by a team of nurses and laboratory technicians trained by local investigators.

All data collected was entered in duplicate on the OpenClinica® database, and statistical analyses were then achieved on software R.

Diagnostic test accuracy was estimated by calculating the total number of true positives (TP), false positives (FP), true negatives (TN), false negatives (FN), sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), with qualitative PCR as the reference test.

Confidence intervals (CI) at 95% for values were calculated, where appropriate.

Kappa (k) values were calculated to measure the level of concordance between diagnostic tests (US-RDT, co-RDT, microscopy) and PCR. The values were interpreted as follows:

- kappa < 0.20: Bad concordance,
- kappa between 0.21– 0.40: Medium concordance
- kappa between 0.41– 0.60: Moderate concordance
- kappa between 0.61– 0.80: Good concordance
- kappa between 0.81–1.00: Very good concordance

P-value ≤0.05 was considered statistically significant.

Participation in the study was subject to the signing of a duly completed informed consent form. Each patient confidentiality was kept. The study research protocol was approved by the Institutional Ethics Committee for Health Research (CEIRS) and the authorization got from Nanoro Health District prior to the recruitment of any participant in the study.

Results

Participants participation

A total of 418 pregnant women were recruited in the study with 25 years as the participants 'median age. Housewives accounted for 77.8% of cases followed by those in the informal sector estimated at 9.3%. Married women accounted for 97.4% of participants. The first antenatal care took place in the 1st, 2nd and 3rd trimesters in respectively 7.4%, 70.6% and 22% of cases with a median gestational age of 25 weeks' amenorrhea. 81.3% of cases had no functional signs of malaria at their first

prenatal visit.

Prevalence of malaria

The prevalence of malaria according to US-RDT was slightly below that with co-RDT. It was respectively estimated at 45% with US-RDT and at 45.5% with co-RDT. The prevalence of thick blood smears and PCR was respectively estimated at 28.2% and 47.4%. *Plasmodium falciparum* was the only species responsible for malaria infection.

Using PCR as the reference method, the prevalence of malaria in asymptomatic pregnant women was estimated at 34.9%, compared with 12.4% in symptomatic women.

Parasitemia ranged from 48 to 17,715 trophozoites/µL (IQR: 222.5 - 2811), with a median value of 759 parasites/µL.

General diagnostic performances of diagnostic tests

❖ **Performance of US-RDT**

The US-RDT has correctly identified 163 out of 198 PCR-positive *P. falciparum cases*, and reported 35 women as negative although they were carrying malaria infection according to PCR. The proportion of false negatives was estimated 17.7%.

The sensitivity of the US-RDT compared with PCR was estimated at 82.3% with a confidence interval (CI) at 95% [76.3 - 87.4]. Its specificity was 88.6% with a CI at 95% [83.7 - 92.5]. Positive and negative predictive values were respectively 86.7% and 84.8% (Table 1).

Figure 1: Performance of US-RDT with PCR as the reference test.

	PCR		Total
	Positive	**Negative**	
US-RDT			
Positive	163	25	188
Negative	35	195	230
Total	**198**	**220**	**418**
	CI at 95%		
Sensitivity (%)	82	[76.3 – 87.4]	
Specificity (%)	88.6	[83.7 – 92.5]	
Positive predictive value (%)	86.7	[81.0 – 91.2]	
Negative predictive value (%)	84.8	[79.5 – 89.2]	

Figure 2: Performance of co-RDT with PCR as the reference test.

	PCR		Total
	Positive	**Negative**	
Co-RDT			
Positive	150	40	190
Negative	48	180	228
Total	**198**	**220**	**418**
	CI at 95%		
Sensitivity (%)	75.8	[69.2 – 81.6]	
Specificity (%)	81.8	[76.1 – 86.7]	
Positive predictive value (%)	78.9	[72.6 – 84.5]	
Negative predictive value (%)	78.9	[73.1 – 84.1]	

❖ **Performance of co-RDT**

Table 2 shows that 48 women were tested negative by co-RDT although they were carrying malaria infection according to PCR. The proportion of false negatives was 24.2%. The sensitivity of conventional RDT was 75.8% with a CI at 95% [69.2 - 81.6]. Its specificity was 81.8% with a CI at 95% [76.1 - 86.7]. Positive and negative predictive values were respectively 78.9% and 78.9%.

❖ **Performance of thick blood smears(TBS)**

Thick blood smears had a sensitivity lower than that of the two rapid diagnostic tests. Compared with PCR, sensitivity was estimated at 56.6%; CI at 95% [49.4 - 63.6]. This difference was significant because their 95% confidence intervals did not intersect. However, the thick blood smears had significantly the best specificity estimated at 97.3%; CI at 95% [94.2 -99.1]. Table 3 summarizes the performance of the thick blood smears.

Positive and negative predictive values were respectively estimated at 94.9% and 71.3%.

Figure 3: Thick blood smears performance based on PCR.

	PCR		Total
	Positive	**Negative**	
Thick blood smears			
Positive	112	6	118
Negative	86	214	300
Total	198	220	418
	CI at 95%		
Sensitivity (%)	56.6	[49.4 – 63.6]	
Specificity (%)	97.3	[94.2 –99.1]	
Positive predictive value (%)	94.9	[89.3 – 98.1]	
Negative predictive value (%)	71.3	[65.9 – 76.4]	

Concordance level of diagnostic tests PCR

The level of concordance between co-RDT and thick blood smears results was moderate as a whole. US-RDT results showed good concordance with those of PCR. Table 4 summarizes the kappa coefficients of the various diagnostic tests.

Figure 4: Concordance level of diagnostic tests.

Diagnostic test	Kappa coefficient	Level of Concordance with PCR
US-RDT	0.71	Good concordance
co-RDT	0.58	Moderate concordance
TBS	0.56	Moderate concordance

Diagnostic test performance in asymptomatic pregnant women

Table 5 shows that US-RDT was more sensitive in detecting malaria infections in asymptomatic women. Its positive predictive value was significantly better than that of co-RDT (respectively estimated at 86.0%, CI at 95% [82.3 - 89.7] and 76.4%, CI at 95% [72.1 - 81.1]). Specificity was significantly better with thick blood smears.

Figure 5: Performance of different diagnostic tests in pregnant women with asymptomatic malaria.

	US-RDT (CI at 95%)	co-RDT(CI at 95%)	TBS (CI at 95%)
Sensitivity (%)	80.1 [75.9–84.4]	71.9 [67.1 – 76.7]	54.8 [49.5 – 60.1]
Specificity (%)	90.2 [87.1–93.4]	83.5 [79.6 – 87.4]	96.9 [95.1 – 98.7]
PPV (%)	86.0 [82.3 – 89.7]	76.4 [72.1 – 81.1]	93.0 [90.3 – 95.7]
NPV (%)	85.8 [82.1 – 89.5]	79.8 [75.5 – 84.1]	74.0[69.3 – 78.7]

Discussion

Only 7.4% of cases had their antenatal care during the first trimester of pregnancy. Several authors in Burkina Faso have made the same observation about delays in starting antenatal care [7,8]. This delay in antenatal care could be explained by social constraints and beliefs. It is customary in villages to conceal pregnancy; as certain evil spirits could harm the fetus. So, they believe that when the uterus reaches a certain size, visible to everyone, there are fewer risks. This delay in the first consultation considerably limits the potential of antenatal care.

In this study, blood samples were taken from all pregnant women. The general prevalence of malaria as determined by US-RDT, co-RDT and PCR was relatively similar (respectively estimated at 45%, 45.5% and 47.4%). However, significant discrepancies between microscopic examination and US-RDT were identified with a prevalence respectively reaching 28.2% and 45%. The role of microscopic examination as the gold standard for malaria diagnosis is increasingly questioned because of false-negative results at low parasitaemia levels (less than 20 to 30 parasites/µL of blood) [9,10].

The prevalence of asymptomatic malaria during the first antenatal visit was estimated at 34.9% with PCR as the reference standard. These values are paradoxically lower than the 54% reported by Kattenberg et al in 2011 [11] in the same locality. Asymptomatic infection is one of characteristic in the highly transmitted areas of malaria; therefore, we would expect a prevalence similar to that found by Kattenberg et al. In our study, the prevalence of asymptomatic P. falciparum infection may have been somewhat lower because of the sensitivity of the PCR technique used. In addition, women living in malaria-endemic areas are continually exposed to Plasmodium. They have developed partial immunity, which can lead to persistent low-grade infection, reducing the presence of typical malaria symptoms such as fever and anemia [12,13].

With a sensitivity of 82.3%, the US-RDT Alere had a significantly greater ability to make the distinction between healthy and sick individuals, compared with thick blood smears. However, this sensitivity is below that recommended by WHO estimated at 95%.

The higher sensitivity of US-RDT Alere (compared with microscopy and co-RDT) makes it potentially more useful in field surveys mapping malaria prevalence to orientate malaria national and international intervention efforts.

The positive predictive value is also an important parameter to be considered even though sensitivity is crucial in reassuring end-users about the low probability of US-RDT to miss a malaria infection. As a whole, US-RDT showed a lower PPV than thick blood smears (86.7% against 94.9%).

Our results also have showed that US-RDT had a better sensitivity (80.1% and CI at 95% [75.9-84.4]) for detecting malaria infections among asymptomatic women. Our study confirmed the results of a large field survey conducted in Myanmar in which US-RDT has detected more asymptomatic parasites than co-RDT and microscopy [14]. As most infections are asymptomatic in pregnant women, the systematic use of US-RDT during antenatal visits could help in detecting and treating infections in order avoid the consequences of malaria for both the mother and fetus.

Conclusion

The performance of US-RDT was better than co-RDT for diagnosing both symptomatic and asymptomatic malaria. To date, most of the studies published in Africa on the US-RDT have been carried out in reference laboratories controlled by highly qualified personnel. Evaluation under field conditions by public health workers will be necessary to assess its applicability in routine diagnosis within resource-limited settings.

Ethics approval and consent to participate

Participation in the study was subject to the signing of a duly completed informed consent form. Each patient confidentiality was kept. The study research protocol was approved by the Institutional Ethics Committee for Health Research (CEIRS) and the authorization got from Nanoro Health District prior to the recruitment of any participant in the study.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Conflict of interest

The authors declare that they have no competing interests in this section.

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This research did not receive any specific grant from funding agencies.

Authors' contribution

All Authors conceptualized, designed the study, collected, analyzed, and interpreted the data, and also drafted the manuscript. Data analysis, drafting of the manuscript, and advising

the whole research paper and also involved in the interpretation of the data and contributed to manuscript preparation. All authors read and approved the final manuscript.

References

1. Oumarou ZM, Lamine MM, Issaka T, Moumouni K, Alkassoum I, et al. Malaria infection during pregnancy in Niamey, Niger. Pan Afr Med J. 2020; 37: 365.

2. Mockenhaupt FP, Bedu-Addo G, Eggelte TA, Hommerich L, Holmberg V, et al. Rapid Increase in the Prevalence of Sulfadoxine-Pyrimethamine Resistance among Plasmodium falciparum Isolated from Pregnant Women in Ghana. J Infect Dis. 2008; 198: 1545-9.

3. Iwalokun BA, Iwalokun SO, Adebodun V, Balogun M. Carriage of Mutant Dihydrofolate Reductase and Dihydropteroate Synthase Genes among Plasmodium falciparum Isolates Recovered from Pregnant Women with Asymptomatic Infection in Lagos, Nigeria. Med Princ Pract. 2015; 24: 436-43.

4. Agudelo O, Arango E, Maestre A, Carmona-Fonseca J. Prevalence of gestational, placental and congenital malaria in northwest Colombia. Malar J. 2013; 12: 341.

5. Slater HC, Ross A, Ouédraogo AL, White LJ, Nguon C, Walker PGT, et al. Assessing the impact of next-generation rapid diagnostic tests on Plasmodium falciparum malaria elimination strategies. Nature. 2015; 528: S94-101.

6. Das S, Jang IK, Barney B, Peck R, Rek JC, et al. Performance of a High-Sensitivity Rapid Diagnostic Test for Plasmodium falciparum Malaria in Asymptomatic Individuals from Uganda and Myanmar and Naive Human Challenge Infections. Am J Trop Med Hyg. 2017; 97: 1540-50.

7. Ouédraogo A, Tiono AB, Diarra A, Bougouma ECC, Nébié I, et al. Transplacental transmission of Plasmodium falciparum in a highly malaria endemic area of Burkina Faso. J Trop Med. 2012.

8. Tahita MC, Tinto H, Menten J, Ouedraogo JB, Guiguemde RT, et al. Clinical signs and symptoms cannot reliably predict Plasmodium falciparum malaria infection in pregnant women living in an area of high seasonal transmission. Malar J. 2013; 12: 1-7.

9. Vásquez AM, Medina AC, Tobón-Castaño A, Posada M, Vélez GJ, et al. Performance of a highly sensitive rapid diagnostic test (HS-RDT) for detecting malaria in peripheral and placental blood samples from pregnant women in Colombia. PLOS ONE. 2018; 13: e0201769.

10. Kimura M, Miyake H, Kim HS, Tanabe M, Arai M, Kawai S, et al. Species-specific PCR detection of malaria parasites by microtiter plate hybridization: clinical study with malaria patients. J Clin Microbiol. 1995; 33: 2342-6.

11. Kattenberg JH, Tahita CM, Versteeg IAJ, Tinto H, Traoré/Coulibaly M, D'Alessandro U, et al. Evaluation of Antigen Detection Tests, Microscopy, and Polymerase Chain Reaction for Diagnosis of Malaria in Peripheral Blood in Asymptomatic Pregnant Women in Nanoro, Burkina Faso. Am J Trop Med Hyg. 2012; 87: 251-6.

12. Unwin VT, Ahmed R, Noviyanti R, Puspitasari AM, Utami RAS, et al. Use of a highly-sensitive rapid diagnostic test to screen for malaria in pregnancy in Indonesia. Malar J. 2020; 19: 28.

13. Vélez G, Vásquez AM, Medina A, Serra-Casas E, Campillo A, et al. Evaluation of highly sensitive diagnostic tools for the detection of P. falciparum in pregnant women attending antenatal care visits in Colombia. BMC Pregnancy Childbirth. 2020; 20: 1-11.

14. Landier J, Haohankhunnatham W, Das S, Konghahong K, Christensen P, et al. Operational Performance of a Plasmodium falciparum Ultrasensitive Rapid Diagnostic Test for Detection of Asymptomatic Infections in Eastern Myanmar. J Clin Microbiol. 2018; 56: e00565-18.