FUDMA Journal of Sciences (FJS)
ISSN online: 2616-1370
ISSN print: 2645 - 2944
Vol. 8 No. 3, June, (Special Issue) 2024, pp 462 - 468
DOI: https://doi.org/10.33003/fjs-2024-0803-2583

PERSISTENCE POSITIVITY OF LACTATE DEHYDROGENASE RAPID DIAGNOSTIC TESTS ANTIGENS IN PREGNANT WOMEN AFTER ANTIMALARIA TREATMENT IN SOME HOSPITALS IN KATSINA

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ABSTRACT

Malaria is a life-threatening disease caused by parasites transmitted to people through the bites of infected female Anopheles mosquitoes. It is preventable and curable. This study investigates the persistent positivity of Lactate Dehydrogenase (pLDH) Rapid diagnostic tests antigens in pregnant women after antimalarial treatment. The study was conducted in Turai Yaradua Maternity and Children's Hospital Katsina and Federal Medical Centre Katsina. Samples were collected with the help of trained physicians. The result from this study shows that lactate dehydrogenase antigen persists in the blood after treatment with fensider (antimalaria drug). After administering the drug to the pregnant women found to be positive for malaria, it was observed that in all the age groups, day 3, day 7, and day 14 post-drug treatment were all still positive for malaria using the pLDH malaria rapid diagnostic tool. It was also observed that after 21 days post-treatment, all the different age groups were still positive for malaria except those aged 45 to 50 (95.0%). There is no statistically significant difference between the age of pregnancy $p>0.05$. The percentage positivity of pLDH started changing day 21 in 3rd trimester and the change peak at day 28 post-drug treatment in all three trimesters. There is no statistical significance difference between the age of pregnancy $p>0.05$. However, the first trimester shows the highest negative result (66.7%). It also shows that age, tribe, trimester of pregnancy, and occupation were statistically not associated with the persistence positivity of the pLDH. The parasite density might be responsible for the persistence and positivity of proteins.

Keywords: Malaria, Lactate Dehydrogenase, Pregnant women

INTRODUCTION

Malaria is a life-threatening disease caused by parasites transmitted to people through the bites of infected female *Anopheles* mosquitoes. It is preventable and curable. In 2019, there were an estimated 229 million cases of malaria worldwide and 409,000 estimated deaths (WHO, 2020). Children under 5 years and pregnant women are the most vulnerable group affected by malaria; in 2019, they accounted for 67% (274,000) of all malaria deaths worldwide (WHO, 2020). The African Region carries a disproportionately high share of the global malaria burden. In 2019 the region was home to 94% of malaria cases and deaths (WHO, 2020). Total funding for malaria control and elimination reached an estimated US$ 3 billion in 2019. Contributions from governments of endemic countries amounted to US$ 900 million, representing 31% of total funding (WHO, 2020).

Malaria is an acute febrile illness. In a non-immune individual, symptoms usually appear 10-15 days after the infective mosquito bite. The first symptoms are fever, headache, and chills which may be mild and difficult to recognize as malaria. If not treated within 24 hours, *P. falciparum* malaria can progress to severe illness, often leading to death (WHO, 2020).

Accurate diagnosis is essential for effective malaria treatment. Rapid diagnostic tests (RDTs) such as the histidine-rich protein II (HRP-II) and lactate dehydrogenase (LDH) tests are commonly used methods to identify malaria infections. However, the reliability of these tests may be affected by factors such as the persistence of parasite antigens in the body after treatment (Falade, 2016).

Accurate diagnosis plays a crucial role in the effective treatment of malaria, especially given the increasing prevalence of drug-resistant strains (WHO, 2020). Early and precise identification of the parasite is vital for appropriate treatment selection and patient management. Historically, the gold standard for malaria diagnosis has been microscopy, but this method has limitations in terms of sensitivity, particularly in cases of low parasitemia (Falade, 2016). Rapid diagnostic tests (RDTs) have emerged as a valuable alternative, offering quick and reliable results, however, the accuracy of RDTs in detecting malaria antigens can be compromised after antimalarial treatment, leading to false-negative results and delayed appropriate therapy. This problem is particularly relevant in pregnant women due to physiological changes that occur during pregnancy (Amoah *et al.*, 2016). The retention of Histidine-Rich Protein II (HRP-II) and Lactate Dehydrogenase (pLDH) rapid diagnostic tests (RDTs) in pregnant women after antimalarial treatment is a significant problem in the diagnosis of malaria. Previous studies have shown that pregnant women are at an increased risk of malaria infection due to their immunocompromised state (WHO, 2011). This study on the retention of lactate dehydrogenase RDTs in pregnant women after antimalaria treatment therefore aim at determining the extent and duration of RDTs' non-retention of antigens in this population and understanding the variations in RDT results in pregnant women. This will contribute to improved malaria diagnosis and treatment guidelines in vulnerable populations.

MATERIALS AND METHODS

The Study Area

The study was conducted in Turai Yaradua Maternity and Children's Hospital Katsina and Federal Medical Centre Katsina, Katsina State. Katsina State is located on the coordinates $12^{0}15^{`}$N and $7^{0}30^{`}$E. It has a population of 10,368,500 (2022 projection) and covers an area of 24,192 Km^2. It has an elevation of 519mts above sea level, with an international boundary in the north to the Niger Republic. It also shares a border in the East with Kano and Jigawa States, the West with Zamfara State, and the South with Kaduna State.

Sample Collection
Samples were collected from pregnant women attending antenatal care at Turai Yar'Adua Maternity and Children's Hospital, Katsina, and Federal Medical Centre Katsina. Samples were collected with the help of trained physicians.

Inclusion Criteria
The inclusion criteria for enrollment include; pregnant women visiting the hospital for antenatal care. Pregnant women who gave their consent. Pregnant women who were positive for malaria parasite.

Sample Size Determination
Blood Sample size for the study was determined using Slovin's formula was used to determine the sample size (Ellen, 2018).
$n=N\div (1+Ne^2)$
Where, n = Number of samples required,
N = Total population = 5,801,584
e = Error tolerance, at the confidence level of 95 percent, the margin error is 0.05.
$n = 5{,}801{,}584 \div [1+ 5{,}801{,}584(0.05^2)] = 400$

Ethical Clearance and Informed Consent
Ethical clearance was obtained from the ethical and human research committee of Katsina State Ministry of Health. Consent of all participating individuals was obtained following the standards of human experimentation and with the Helsinki Declaration of 1975, as revised in 2008 (Helsinki, 2008).

Study Design
Only pregnant women who tested positive for malaria were used for the study. Pregnant women who tested positive for malaria parasite were given a single dose treatment with fansidar and supervised by qualified medical personnel. The tests for malaria were repeated on days 3, 7, 14, 21, 28, 35, and 42 days after treatment until some of the RDTs became negative. Follow-up lasted for 42 days.

Malaria Diagnosis Using Rapid Diagnostic Test
The samples were collected by pricking the finger. A gentle prick was made on the tip of the finger with a sterile lancet at the disinfected site. Using the blood collection device provided in the RDTs kit, a required volume of blood was collected. The collected blood was transferred to the sample well on the RDT cassette, 2 drops of buffer were added into the buffer well, and waited for 15 minutes before the result was taken. The sample collection and processing were conducted concurrently. The patient's information and RDT results were recorded in the appropriate register. The sample collection has a span of 3 months, starting in September 2021 and ending in November 2021.

Treatment
Pregnant women who tested positive for malaria parasite were given a single dose treatment with fansidar and supervised by qualified medical personnel.
Fansidar tablet is an antiparasitic drug used for the treatment of malaria especially in pregnant women, each tablet containing 500mg1 – (5,6-dimethoxy-4-pyrimidiny) sulfanilamide (sulfadoxine) and 25 mg 2,4-diamino-5-(p-chlorophenyl) -6-ethyl pyrimidine (pyrimethamine). Each tablet also contains cornstarch, gelatin, lactose, magnesium stearate, and talc.

Data Analysis
Data obtained were entered using Microsoft Excel. Descriptive statistics were performed for different demographic characteristics. The chi-square test was used to test the level of significance among categories such as age group, gender, occupation, etc. Bivariate and multivariate logistic regressions were performed to measure the likelihood of infection in the different categories. All analyses were performed using the Statistical Package for Social Sciences (SPSS) version 21. All analyses were performed at $p<0.05$.

RESULTS AND DISCUSSION

Demographic Characteristics of the Pregnant Women Who Participated in the Study
Table 1 summarizes the demographic characteristics of the pregnant women who participated in the study. It was observed that the age group 15-19 has the highest number of participants (17.5%) and the age group >50 has the lowest number of participants (1.3 %.). According to the age of the pregnancy, the highest number of participants examined were in the third trimester with 45%, it was observed that the tribe with the highest number of participants is Hausa (71%) whereas Kanuri has the lowest number of participants (0.8%). Housewife has the highest number of participants (40.8%).

Table 1: Demographic Presentation of the Pregnant Women Who Participated in the Study

Demographic Characteristics	Number Examined (%)
Age Groups (Years)	
15 – 19	42 (17.5)
20 – 24	35 (14.6)
25 – 29	34 (14.2)
30 – 34	40 (16.7)
35 – 39	32 (13.3)
40 – 44	34 (14.2)
45 – 49	20 (8.3)
> 50	3 (1.3)
Total	**240 (100%)**
Age of Pregnancy	
1st Trimester	48 (20.0)
2nd Trimester	84 (35.0)
3rd Trimester	108 (45.0)
Total	**240 (100%)**
Tribe	
Fulani	36 (15.0)

Hausa	171 (71.3)
Igbo	8 (3.3)
Kanuri	2 (0.8)
Nupe	4 (1.7)
Yoruba	19 (7.9)
Total	**240 (100%)**
Occupation	
Business	48 (20.0)
Teaching	4 (1.7)
Housewives	98 (40.8)
Students	37 (15.4)
Civil Service	53 (22.1)
Total	**240 (100.0)**

Age of Pregnant Women that Remain Positive for Plasmodium Lactate Dehydrogenase Rapid Diagnostic Test after Treatment with Antimalarial Drugs

Table 2 summarizes the percentage prevalence in the positivity of different age groups of pregnant women that participated in the study after administering drugs to those found to be positive for malaria, it was observed that at days 3, 7, and 14 post-treatment they were all positive. At days 21 and 28 post-treatment it was observed that all the pregnant women were still positive except in the age group 45-49 (95.0%). However, on day 35, the percentage in the positivity result changed in almost all the groups except the age group >50 which was still 100%. Moreover, the percentage of the positivity result changed in all the age groups on day 42. There was no statistically significant difference between all the age groups P>0.05, hence age group 20 – 24 shows the highest negative result 61% in day 42 post-treatment as observed in Table 2.

Table 2: Age of Pregnant Women That Remain Positive Using Plasmodium Lactate Dehydrogenase Rapid Diagnostic Test after Treatment with Antimalarial Drugs

Age Groups	Number Examined	Number Tested Positive (%) for PLDH						
		Day 3	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42
15 – 19	42	42 (100.0)	42 (100.0)	42 (100.0)	42 (100.0)	40 (95.2)	34 (81.0)	27 (54.3)
20 – 24	35	35 (100.0)	35 (100.0)	35 (100.0)	35 (100.0)	34 (97.1)	30 (85.7)	21 (60.0)
25 – 29	34	34 (100.0)	34 (100.0)	34 (100.0)	34 (100.0)	32 (94.1)	27 (79.4)	18 (52.9)
30 – 34	40	40 (100.0)	40 (100.0)	40 (100.0)	40 (100.0)	39 (97.5)	38 (95.0)	25 (62.5)
35 – 39	32	32 (100.0)	32 (100.0)	32 (100.0)	32 (100.0)	32 (100.0)	29 (90.6)	24 (75.0)
40 – 44	34	34 (100.0)	34 (100.0)	34 (100.0)	34 (100.0)	33 (97.1)	27 (79.4)	19 (55.9)
45 – 49	20	20 (100.0)	20 (100.0)	20 (100.0)	19 (95.0)	19 (95.0)	16 (80.0)	11 (55.0)
> 50	3	3 (100.0)	3 (100.0)	3 (100.0)	3 (100.0)	3 (100.0)	3 (100.0)	2 (66.7)
Total	**240**	**240 (100.0)**	**240 (100.0)**	**240 (100.0)**	**239 (99.6)**	**232 (96.7)**	**204 (85.0)**	**147 (61.3)**
χ^2		NA	NA	NA	11.048	2.458	7.072	4.529
Df		NA	NA	NA	7	7	7	7
p Value		NA	NA	NA	0.137ns	0.930ns	0.421ns	0.717ns

NA – Not applicable, df – Degree of freedom, ns – Not significant at p>0.05, pLDH – Lactate Dehydrogenase, χ^2 – Chi-square.

Percentage Prevalence of the Three Stages of Pregnancy after Malaria Diagnosis Using Plasmodium Lactate Dehydrogenase Rapid Diagnostic Test

Table 3 reveals that at day 3, 7 and 14 post treatment they were all positive. It was also observed that at days 21 and 28 both the first and second trimesters were still positive whereas those in the third trimester reduced in their positivity (99.1%). However, the persistent positivity decreases in all the trimesters from 28 days post-treatment. The highest negative positivity was observed in the second trimester at day 42 with 57.1%. There is no statistically significant difference between the age of pregnancy p>0.05.

Percentage Prevalence in different tribes of Pregnant Women that remain Positive for Plasmodium Lactate Dehydrogenase Rapid Diagnostic Test Antigen after Antimalarial treatment

The prevalence in antigen positivity of pLDH in different tribes that participated in the study after administering drugs to pregnant women who were found to be positive for malaria is presented in Table 4. It was observed that in all the tribes days 3, 7, and 14 were all 100% showing that there is no change in the positivity of the pLDH antigens. However, on day 21 there is a decrease in positivity among pregnant women from the Hausa tribe with 99.4%. , It was also observed that after day 28 post-treatment there was a decrease in positivity in Hausa and Fulani with 96.5% and 94.4% respectively. Moreno, at day 35 post-treatment, the percentage of positivity changed in Hausa, Fulani, and Yoruba tribes but remained at 100% in Igbo, Kanuri, and Nupe tribes. Furthermore, the percentage of the positivity of the pregnant women change in all the tribes on day 42 after treatment. There was no statistically significant difference between the tribes p>0.05, however, the Nupe tribe showed the highest negative result (50.0%) on day 42 post-treatment as presented in Table 4.

Table 3: Percentage Prevalence of the Three Stages of Pregnancy after Malaria Diagnosis Using Plasmodium Lactate Dehydrogenase Rapid Diagnostic Test

Age of Pregnancy	Number Examined	Number Tested Positive (%) for pLDH						
		Day 3	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42
1st Trimester	48	48 (100.0)	48 (100.0)	48 (100.0)	48 (100.0)	47 (97.9)	42 (87.5)	32 (66.7)
2nd Trimester	84	84 (100.0)	84 (100.0)	84 (100.0)	84 (100.0)	81 (96.4)	70 (83.3)	48 (57.1)
3rd Trimester	108	108 (100.0)	108 (100.0)	108 (100.0)	107 (99.1)	104 (96.3)	92 (85.2)	67 (62.0)
Total	**240**	**240 (100.0)**	**240 (100.0)**	**240 (100.0)**	**239 (99.6)**	**232 (96.7)**	**204 (85.0)**	**147 (61.3)**
χ^2		NA	NA	NA	1.227	0.294	0.421	1.219
Df		NA	NA	NA	2	2	2	2
p Value		NA	NA	NA	0.541ns	0.864ns	0.810ns	0.544ns

NA – Not applicable, df – Degree of freedom, ns – Not significant at p>0.05, pLDH – Lactate Dehydrogenase, χ^2 – Chi-square.

Table 4: Percentage Positivity of Antigen of Plasmodium Lactate Dehydrogenase detected after Treatment in Different Tribe

Tribe	Number Examined	Number Tested Positive (%) for Pldh						
		Day 3	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42
Hausa	171	171 (100.0)	171 (100.0)	171 (100.0)	170 (99.4)	165 (96.5)	144 (84.2)	106 (62.0)
Fulani	36	36 (100.0)	36 (100.0)	36 (100.0)	36 (100.0)	34 (94.4)	31 (86.1)	21 (58.3)
Yoruba	19	19 (100.0)	19 (100.0)	19 (100.0)	19 (100.0)	19 (100.0)	15 (78.9)	11 (57.9)
Igbo	8	8 (100.0)	8 (100.0)	8 (100.0)	8 (100.0)	8 (100.0)	8 (100.0)	7 (87.5)
Kanuri	2	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	0 (0.0)
Nupe	4	4 (100.0)	4 (100.0)	4 (100.0)	4 (100.0)	4 (100.0)	4 (100.0)	2 (50.0)
Total	**240**	**240 (100.0)**	**240 (100.0)**	**240 (100.0)**	**239 (99.6)**	**232 (96.7)**	**204 (85.0)**	**147 (61.3)**
χ^2		NA	NA	NA	0.405	1.706	3.135	5.956
Df		NA	NA	NA	5	5	5	5
p Value		NA	NA	NA	0.955ns	0.888ns	0.679ns	0.311ns

NA – Not applicable, df – Degree of freedom, ns – Not significant at p>0.05, pLDH – Lactate Dehydrogenase, χ^2 – Chi-square.

Percentage Prevalence of Pregnant Women that Remain Positive for Plasmodium lactate Dehydrogenase Antigen after Treatment with Antimalarial According to Different Occupation

Table 5 shows the prevalence in the positivity of antigen of pLDH diagnostic test kit after treatment with malaria drug in pregnant women who participated in the study in various occupations. It was observed that after days 3, 7, and 14 after taking the antimalarial drugs, they were still positive in all the occupations using pLDH malaria rapid diagnostic stool. After day 21 post-treatment, the positivity changed only in pregnant women who were civil servants with 98.1%, moreover at day 28, the percentage positivity changed in all the occupations except in pregnant women who were teachers which was still 100% However, on day 35 and 42 after antimalarial treatment the percentage positivity change completely in all the occupations. There is no statistical significance between the occupation P>0.05. Hence, the teacher shows the highest negative result with 75.0% on day 42 post-treatment as shown in Table 5.

Table 5: Presentation According to the Occupation of Pregnant Women Positive for Plasmodium Lactate Dehydrogenase

Occupation	Number Examined	Number Tested Positive (%) for PLDH						
		Day 3	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42
Business	48	48 (100.0)	48 (100.0)	48 (100.0)	48 (100.0)	47 (97.9)	43 (89.6)	28 (58.3)
Teacher	4	4 (100.0)	4 (100.0)	4 (100.0)	4 (100.0)	4 (100.0)	3 (75.0)	3 (75.0)
House wife	98	98 (100.0)	98 (100.0)	98 (100.0)	98 (100.0)	93 (94.9)	84 (85.7)	59 (60.2)
Student	37	37 (100.0)	37 (100.0)	37 (100.0)	37 (100.0)	36 (97.3)	29 (78.4)	26 (70.3)
Civil Servant	53	53 (100.0)	53 (100.0)	53 (100.0)	52 (98.1)	52 (98.1)	45 (84.9)	31 (58.5)
Total	**240**	**240 (100.0)**	**240 (100.0)**	**240 (100.0)**	**239 (99.6)**	**232 (96.7)**	**204 (85.0)**	**147 (61.3)**
χ^2		NA	NA	NA	3.543	1.712	2.417	1.974
Df		NA	NA	NA	4	4	4	4
p Value		NA	NA	NA	0.471ns	0.789ns	0.660ns	0.740ns

NA – Not applicable, df – Degree of freedom, ns – Not significant at p>0.05, pLDH – Lactate Dehydrogenase, χ^2 – Chi-square.

Bivariate and Multivariate Analysis of Risk Factors Associated with Malaria detection using Plasmodium Lactate Dehydrogenase Rapid Diagnostic Test in Pregnant Women after Treatment with Antimalarial

Table 6 shows the Bivariate and Multivariate Analysis of risk factors associated with malaria detection using the pLDH diagnostic tool in pregnant women after treatment with SP**.** The age group 35-39 years had the highest likelihood of malaria detection with an odds ratio of 1.500, followed by 15-19 with an odds ratio of 1.039. The likelihood of detection of malaria parasites were least in the age group of 25-29 years with odds ratio of 0.563. Pregnant women in their first

trimester had the highest likelihood of malaria parasite detection than the other two trimesters with an odds ratio of 1.224. Igbo had the highest likelihood of malaria detection with an odd ratio of 7.000, followed by Hausa with an odds ratio of 1.631. The tribe with the least likelihood was Nupe tribe with an odds ratio of 1.000. Teachers had the highest likelihood of malaria detection using the pLDH malaria diagnostic tool with an odds ratio of 2.129. Followed by students with odds ratio of 1.677. The likelihood among businesses had the lowest odds ratio of 0.994. The adjusted odds ratio of the likelihood also identified the higher likelihood of detection of malaria parasite in the age group 35-39, >50, 15-19, and 30-34 with an adjusted odds ratio of 2.073, 1.269, 1.170, and 1.066 respectively., The highest adjusted odds ratio was observed in the first and third trimesters with adjusted odds ratios of 1.339 and 1.062 respectively.

Table 6: Bivariate and Multivariate Analysis of Risk Factors Associated with Malaria Detection Using Plasmodium Lactate Dehydrogenase Rapid Diagnostic Test in Pregnant Women after Treatment with Antimalarial

Demographic Characteristics	Number Examined	pLDH (%)	Odds Ratio (95% C.I.)	Adjusted Odds Ratio (95% C.I.)
Age Groups (Years)				
15 – 19	42	27 (54.3)	1.039 (0.086 - 12.525)	1.170 (0.585 - 2.339)
20 – 24	35	21 (60.0)	0.750 (0.062 - 9.082)	0.941 (0.452 - 1.956)
25 – 29	34	18 (52.9)	0.563 (0.047 - 6.806)	0.672 (0.324 - 1.394)
30 – 34	40	25 (62.5)	0.833 (0.070 - 9.995)	1.066 (0.529 - 2.147)
35 – 39	32	24 (75.0)	1.500 (0.119 - 18.837)	2.073 (0.889 - 4.834)
40 – 44	34	19 (55.9)	0.633 (0.052 - 7.670)	0.772 (0.371 - 1.607)
45 – 49	20	11 (55.0)	0.611 (0.047 - 7.882)	0.755 (0.300 - 1.898)
> 50	3	2 (66.7)	1	1.269 (0.113 - 14.195)
Age of Pregnancy				
1st Trimester	48	32 (66.7)	1.224 (0.599 - 2.502)	1.339 (0.688 - 2.606)
2nd Trimester	84	48 (57.1)	0.816 (0.456 - 1.459)	0.768 (0.447 - 1.319)
3rd Trimester	108	67 (62.0)	1	1.062 (0.630 - 1.791)
Tribe				
Hausa	171	106 (62.0)	1.631 (0.224 - 11.861)	0.796 (0.429 - 1.475)
Fulani	36	21 (58.3)	1.400 (0.177 - 11.083)	0.867 (0.422 - 1.781)
Yoruba	19	11 (57.9)	1.375 (0.158 - 11.938)	0.859 (0.332 - 2.223)
Igbo	8	7 (87.5)	7.000 (0.0397 - 123.354)	4.600 (0.557 - 38.009)
Kanuri	2	0 (0.0)	NA	NA
Nupe	4	2 (50.0)	1	0.628 (0.087 - 4.540)
Occupation				
Business	48	28 (58.3)	0.994 (0.450 - 2.194)	0.859 (0.451 - 1.635)
Teacher	4	3 (75.0)	2.129 (0.208 - 21.844)	1.278 (0.114 - 14.294)
House wife	98	59 (60.2)	1.074 (0.544 - 2.119)	0.928 (0.548 - 1.573)
Student	37	26 (70.3)	1.677 (0.688 - 4.093)	1.602 (0.750 - 3.421)
Civil Servant	53	31 (58.5)	1	0.863 (0.463 - 1.605)
Total	**240**	**147 (61.3)**		

Discussion

Pregnant women were examined for the persistence of Lactate Dehydrogenase (pLDH) using Rapid Diagnostic Tests (RDTs). It was observed that pLDH were detected in the blood for up to 42 days in over 80% and 60% respectively. This observation differs from the report of Poti *et al.* (2019) where they reported that pLDH antigens were positive from 1 to 12 days post-treatment in individuals treated with artemether-lumefantrine and atovaquone-proguanil. Ndour *et al.* (2017) also identified pLDH in infected Red Blood Cells (RBC) isolated from *Plasmodium falciparum* patients 3 days post-artesunate treatment.

The persistence of the pLDH antigen might be due to the clearance of dying and non-viable parasites by the process of erythrocyte pitting in the spleen, in which the parasite is removed by splenic macrophages from an intact RBC that return into circulation as infected RBC (Ndour *et al.* 2017 and Ayona *et al.,* 2006). Poti *et al.,* (2019) also suggested that the slower protein clearance is from the RBC fraction of the blood compared to the plasma part of the blood. They also suggested that parasite DNA may persist in the blood even after parasites are killed. They also added that the antigens of pLDH could be binding to uninfected RBCs in circulation upon its release from infected RBCs, therefore contributing to the persistence of positivity (Poti *et al.* (2019). HRP2 levels in human RBCs seem to be 20 – 40 times greater than in the plasma, and post-parasite clearance and persistence of RDT antigens are slower in RBC fraction than in plasma fraction (Poti *et al.,* 2019). Swarthout *et al.* (2007) reported a similar result, where 73% of cases with the RDT test were still positive for malaria parasite 35 days after treatment.

In Nigeria, a study in children at Ibadan, Oyo State by Michael *et al.* (2021) observed 8 p 0.6% HRP2 antigen persistence in children for up to 28 days post-treatment with Fansidar. This observation is similar to the current findings. Swarthout *et al.* (2007) stated that the positivity might be due to parasite density in the blood. In another study, Iqbal *et al.* (2004), found that 35% of patients still had HRP2 antigenaemia 14 days after treatment. Their findings showed that the persistence of HRP2 was as high as 90.4% on day 3 with a gradual decrease to 34.9% by day 14. They also reported that HRP2-based RDTs present more false positive results than

pLDH-based RDTs. Mayxay *et al.* (2001) reported that 61% of patients were positive using pLDH -based RDT tests for than two weeks after initiation of treatment. In Africa, a study by Hopkins *et al.* (2007) in Kampala, Uganda reported that the other RDT assay showed superior sensitivity but inferior specificity compared with the pLDH assay. This observation confirmed the current study as to why more false positive was reported using other RDTs than pLDH. Hopkins *et al.* (2007) stated that the variation in high detection of other malaria RDTs to pLDH was due to its ability to detect at low parasite densities. Also, non-falciparum infections might have contributed to false-negative results for both RDTs. Abeku *et al.* (2008) observed that the variability in the performance of the RDTs might be due to climatic conditions which affects the stability of the devices. Abeku *et al.* (2008) further stated that the malaria RDTs antigens can remain in blood for over 30 days after clearance of the parasites, and the persistence has been shown to depend on the presence of the antigen in erythrocytes and parasite density at the initiation of treatment. Kozycki *et al.* (2007) in their study in Rwanda also reported that other malaria based RDTs were more sensitive than pLDH-based RDTs. This is consistent with the current study. This might also be responsible for the variation observed in the performance of the RDTs used in this study in terms of sensitivity. Kozycki *et al.* (2017) also mention that the density of *Plasmodium falciparum* might be responsible for variation between two RDTs as below the threshold for detection may lead to many false-negative RDTs. Alemayelu *et al.* (2021) reported that deletion of the HRP2 gene can lead to discordant reports in the usage of diagnostic tools in post-treatment diagnosis. Different Rapid diagnostic tests have high variability in performance that is likely due to inadequate quality of manufacturing, incorrect storage and handling, and sometimes poor study methods, analysis, and reporting (Moody, 2002; Tidi and Akogun, 2005; Laurent *et al.*, 2010; Ly *et al.*, 2010).

Abeku *et al.* (2008) reported that the sensitivity of RDTs was not affected by the age of patients or fluctuation in parasites during different months but by parasite density. In their study, they reported that patients with high parasite densities were more likely to test positive than those with low parasitaemia. A study by Alemayelu *et al.* (2021) reported a non-significant difference in the prevalence of malaria RDTs used among age groups of the study population in Assosa zone, Ethiopia. They observed fluctuations in the prevalence among the age groups. This is similar to the observation of the current study. Age is not significantly associated with pLDH protein prevalence. In another study by Oladosu *et al.* (2021) in Osun State, Nigeria, the prevalence of malaria parasites using malaria RDTs showed no significant difference among the age groups of the participants whose age group ranged from 15 to 50 years. This conforms with this study. Houmsou *et al.* (2011) carried out a study in Gboko, Benue state, and reported that the age group of 1 – 10 years and 51-60 years had a higher prevalence of 52.9% and 43.8% respectively, however, no significant difference was observed in malarial infection among the age groups. In this study, the trimester, tribe, and occupation of pregnant women were significantly not associated with the persistence of pLDH. However, a study by Kattenburg *et al.* (2012) in Nanoro, Burkina Faso reported a statistically significant difference in the persistence of pLDH persistence between primigravidae and multigravidae, and also between pregnant women below the age of 25 years and those greater than or equal to 25 years. In their report, primigravidae women had high parasite density than multigravidae, while pregnant women less than the age of 25 years had higher parasite density than those above the age of 25 years. They attributed the differences to parasite density.

Lactate Dehydrogenase RDTs may be useful in diagnosing peripheral *P. falciparum* infections in symptomatic pregnant women. However, they are not sufficiently sensitive for use in screening amongst asymptomatic women. These findings have implications for the management of malaria in pregnancy. The adverse impact of infections detected multiple times even after clearance can lead to multiple treatments which can result in other complications in pregnancy.

CONCLUSION

The result from this study shows that lactate dehydrogenase persists after treatment with fansider (antimalaria drug) in pregnant women. The proteins of pLDH persisted for up to 42 days post-antimalarial treatment. The age groups had no changes in the positivity after days 3, 7, and 14 post-drug treatment for the RDTs, the positivity starts changing after 21 days post-drug treatment. The results of the research also indicate that the sensitivity of pLDH-based RDTs is lower. Age, tribe, trimester of pregnancy, and occupation were statistically not associated with the persistence of pLDH.

It is recommended that expert microscopy should be employed as a modality for post-treatment diagnosis of malaria in pregnancy especially during periods of high transmission of malaria in endemic communities.

The specificity of pLDH can be affected by a series of environmental factors, therefore when deployed, proper maintenance in its storage, and transport, should be carefully monitored.

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