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Research Article

Exploring Barriers of Adherence to Artemisinin- Based Combination Therapy (Act) With One Day Primaquine Treatment for Plasmodium Falciparum Malaria and Compliance to Vector Control Among Marginalized Tribal Communities in East Central India

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Abstract

Background: Artemisinin Based Combination Therapy (ACT) compounds, have been observed to produce rapid therapeutic response, introduced over the past few years against chloroquine resistant Plasmodium falciparum. In India, malaria treatment by Accredited Social Health Activists (ASHAs) in remote and tribal villages has expanded the use of ACTs for the management of uncomplicated malaria. To maximize its effectiveness, patients' adherence to the treatment regimen is central. Measures should therefore be taken to ensure and monitor the use of ACT to avoid the emergence of resistance/treatment failure. The present study assessed the level of adherence to ACT treatment, including the respondents' compliance to vector control interventions.

Methods: The research team visited the houses of pre-diagnosed P. falciparum infected malaria patients, treated by the Community Health Centers with ACT plus primaquine, on the 4th day post treatment. Adherence to the drug regimen was observed on the spot and the patients were interviewed using a semi-structured questionnaire on malaria and their compliance to the ongoing vector control intervention. Rapid diagnostic tests and peripheral blood smear collection were conducted to ascertain whether the patient was cleared of parasitemia post treatment.

Results: 76.5% of the patients were found adhering to the drug regimen. Over 80% of the respondents informed mosquito that bite was one of the causes of malaria and felt it is a serious disease. Only 0.7% of the respondents preferred traditional to ACT medicines for malaria treatment. Lack of space, damaged nets, and use of mosquito repellents were the major reasons of the non-usage of Insecticide-Treated Nets (ITNs). Only 1.6% of the respondents had permitted for indoor residual spray (IRS) in all rooms of their houses. 27.3% of the respondents had permitted spraying their houses partially.

Conclusion: Too many tablets was the major reason for non-adherence to the ACT regimen. Strengthening information, education, and communication/behaviour change communication could enhance drug adherence, improving LLIN use rate, and acceptance to IRS. One of the important take away from the current study was the paradigm shift in preference to ACT from traditional medicines for malaria treatment.

Key Words: malaria; ACT; adherence; LLIN; IRS; traditional medicine; primaquine; tribes; resistance

1.Introduction

Plasmodium falciparum contributes 97% of the malaria incidence globally. Control of malaria relies on vector-control interventions such as Insecticide-Treated Nets (ITNs) and indoor residual spray (IRS) of insecticides, and antimalarial drugs due to nonavailability of an effective vaccine [1]. India

recorded 50.7% (n=338,494 cases) of the malaria cases in the South-East Asia region (n= 667916 cases) and 46% of them are due to P. falciparum during 2019 [2]. The emergence of resistance and subsequent treatment failure against Plasmodium falciparum infection, has limited the use of Chloroquine (CQ) which was used as the first-line treatment for malaria in developing countries. Factors like incorrect dosing, non-compliance with the duration of the dosing regimen, poor drug quality, and drug interaction could have been contributing factors to chloroquine treatment failures [3]. A new group of antimalarials, the Artemisinin Based Combination Therapy (ACT) compounds, have been observed to produce a rapid therapeutic response was introduced during the past eleven years against CQ resistant Plasmodium falciparum [4]. The World Health Organization (WHO) currently recommends six ACTs: artemether-lumefantrine (AL), artesunate-amodiaquine (AS-AQ), artesunate-mefloquine (AS-MQ), artesunate-pyronaridine (AS-PND), artesunate-sulfadoxine/pyrimethamine (AS-SP), and dihydro-artemisinin-piperaquine (DHA-PPQ) [5]. The role of the artemisinin compound is to reduce the parasite load rapidly during the first days of treatment while the role of the partner drug is to eliminate any remaining parasites. [6]. In line with WHO recommendations, nearly all high-burden South East Asian countries including India have moved from chloroquine to ACTs as the first-line treatment of uncomplicated P.falciparum malaria. For the first-line treatment of falciparum malaria, by 2012, 79 out of 88 endemic countries adopted ACT [7] and is proven to be cost effective for malaria treatment [8].

WHO acknowledges the fact that rational use of antimalarial medicines is critical; it suggests that resistance to the ACTs could have a negative impact on national malaria control programmes [9]. Thus, incomplete elimination of parasites exposes the patient to recurrent malaria attacks increasing mortality and health care costs [10]. At the community level, it leads to the development of parasite resistance, precipitating malaria morbidity and mortality [10]. Poor adherence to anti-malaria medications could play a role in the future development of drug resistance. As such, identifying ways to improve anti-malarial compliance will help mitigate drug resistance [11].

However, there is a wide variation among the estimates of treatment adherence [12, 13]. It varies from 1.5% to 100% across different study settings, regimens, treatment duration, study designs and methods [13]. As per WHO report, even if malaria patients are infected with artemisinin partial resistant parasites, nearly all patients treated with an ACT are completely cured provided that the partner drug is highly efficacious in that geographical area. Even when a parasite is partially resistant to artimesinin but non-resistant to the partner drug, then there is a rare chance of treatment failure.

In the absence of partner drug resistance, artemisinin partial resistance rarely leads to treatment failure. [14]. A study conducted at the Thai-Cambodian border, reported the decreased potency of ACTs [15]. Fairhurst RM et al (2016) indicated the development of the malaria parasite's resistance towards the ACTs [16].

In 2010, National center for Vector Borne Disease Control (NCVBDC) in India adopted ACT (Artesunate with Sulphadoxin and Pyremethamine) for P. falciparum malaria treatment [17] and is recommended for uncomplicated malaria treatment [18]. Malaria treatment by Accredited Social Health Activists (ASHA) in the remote and tribal villages of India, has led to an expansion of ACTs for the management of malaria as they are easily available in the village, free of cost [19].

In India, as per the National Drug Policy on malaria 2013, artesunate (AS) tablets are given for three days and sulfadoxine-pyrimethamine (SP) tablets are given on the first day. In addition, primaquine (PQ) tablets are given on the second day. All tablets for a day should be taken together, and swallowed with water after intake of food [20]. To maximize its effectiveness, patients' adherence to the treatment guideline is central [12, 13]. Measures should therefore be taken to ensure and monitor its rational use to avoid the emergence of resistance. Research data assessing patient related factors that affect adherence to antimalarial medication are scanty. Only a few studies have explored adherence and patients' knowledge on cause and treatment aspects of malaria and its treatment.

The efficacy of sulfa–pyrimethamine as a partner drug with Artemisinin for the treatment of P falciparum was reduced in recent studies, largely in northeast India [21]. Based on these results, in January 2013 the expert committee of the National Vector Borne Disease Control Programme (currently known as the National Center for Vector Borne Diseases Control) formulated the first sub-national drug policy for India and selected artemether plus lumefantrine as the new first-line treatment in the northeast and recommended for continued monitoring of anti-malarial drug efficacy for effective malaria control [22].

Odisha State contributes 41.2% of the P. falciparum malaria cases to the national burden during 2017 [2]. Among the 30 districts of Odisha State, Koraput had the fourth highest burden and incidence of falciparum malaria. Prior studies conducted by the Indian Council of Medical Research-Vector Control Research Centre (ICMR-VCRC) during 2013 indicated a high prevalence of afebrile parasitaemia (80%) and gametocytes (8%) [23], which could have led to non-adherence to malaria treatment.

The current study was carried out to assess the level of adherence to the three days ACT and one day primaquine treatment among the P. falciparum infected patients including the community compliance to vector control intervention (LLINs and IRS) measures in general and to identify the factors that make it difficult for patients to take their treatment as per the schedule and the extent of adherence among children below 17 years.

Methodology

Study area

The study was carried out in 2 malarias endemic CHCs (Bandhugaon and Narayanpatna) of Koraput district, Odisha State, India. Malaria data for the past 5 years is furnished in table 1.

Sl. No.	Name of the CHC	Annual parasite incidence (API)				
		2016	2017	2018	2019	2020
1	Bandhugaon	106.81	87.11	20.90	17.62	17.57
2	Narayanpatna	168.40	174.58	36.13	21.24	13.58
3	Laxmipur	58.19	63.65	6.54	4.28	3.62
4	Dasmantpur	51.90	47.22	3.58	2.63	0.94
5	Mathalput	8.54	8.62	2.21	1.19	0.46
6	Kunduli	5.41	8.24	1.07	0.62	0.33
7	Pottangi	27.75	39.48	3.61	3.40	2.64
8	Nandapur	13.25	9.47	1.04	0.89	0.18
9	Lamtaput	67.53	45.84	5.81	4.00	3.12
10	Boipariguda	29.97	15.02	7.20	2.98	2.23
11	Kundura	25.45	16.26	3.99	3.44	2.86
12	Rabanaguda	13.34	10.34	1.27	1.02	0.67
13	Borigumma	7.47	5.58	0.83	0.55	0.22
14	Kotpad	8.49	3.61	1.50	0.57	0.3

Table 1: CHC wise malaria data (API) of Koraput district, Odisha State.

Koraput district (18o13' and 19o10'N and 82o5' and 83o13'E) is situated in the southern part of Odisha, bordered by states of Andhra Pradesh on the eastern side and Chhattisgarh on the Western side. The district spans an area of 8807sq km (Figure 1). Many rivulets crisscross the valley and joins the larger rivers, Bansadhara and Kolab. The district has 2028 revenue villages and is inhabited by about 1.4 million population, of which 50% are constituted by the local tribes. The district is home to 13 tribes among them Kondhs, Ghadavas and Parajas are primitive. These tribes reside in huts in small hamlets / clusters located on hilltops and foothills. The literacy rate is 35.72%. The majority of the villagers are agricultural labourers and marginal farmers. During summer, villagers go to the forest and collect forest products, that include timber, firewood, bamboo, kendu leaf, sal leaf, Mohul flowers/fruit, etc. During rainy and winter seasons most of them work as agricultural labourers away from their homes on a daily wage. Lack of basic infrastructure (communication, transport, roads and paths) makes it difficult to reach village in quicktime. (Source: District hand book, Koraput, 2009), Among the 14 CHCs of Koraput district, Narayanapatna and Bandhugaon CHCs were severely affected by malaria, that was contributing >60% of the P. falciparum cases (Figure 2), over past several decades (Source: CDMO Office, Koraput). Therefore, we thought it worthwhile to conduct the study in these two Community Health Centre (CHCs).

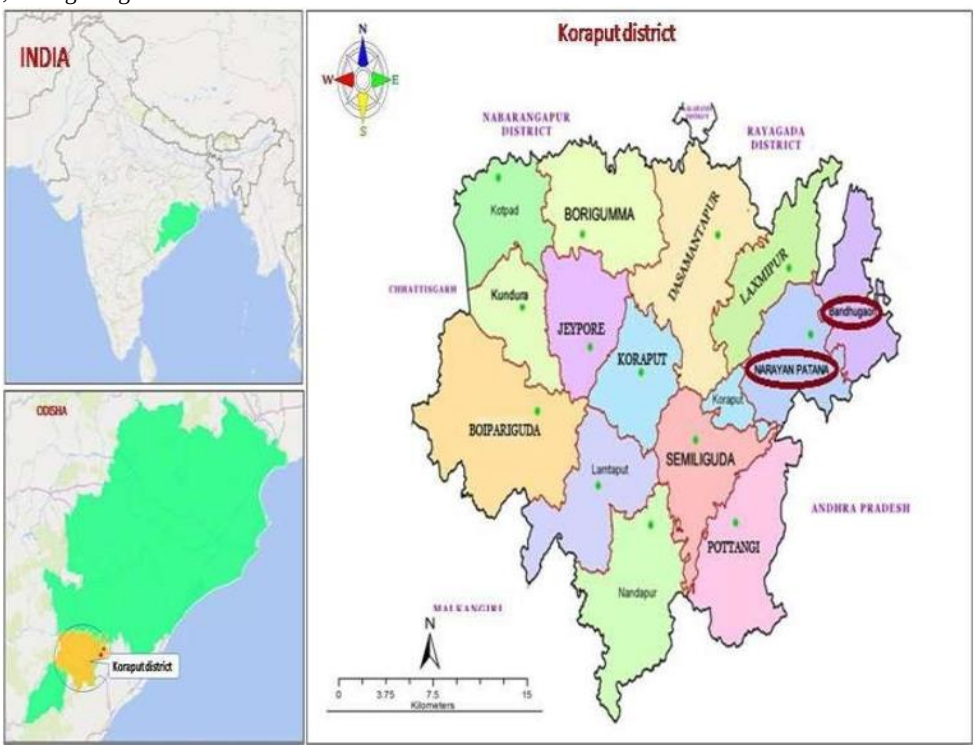

Figure 1: Map showing study area.

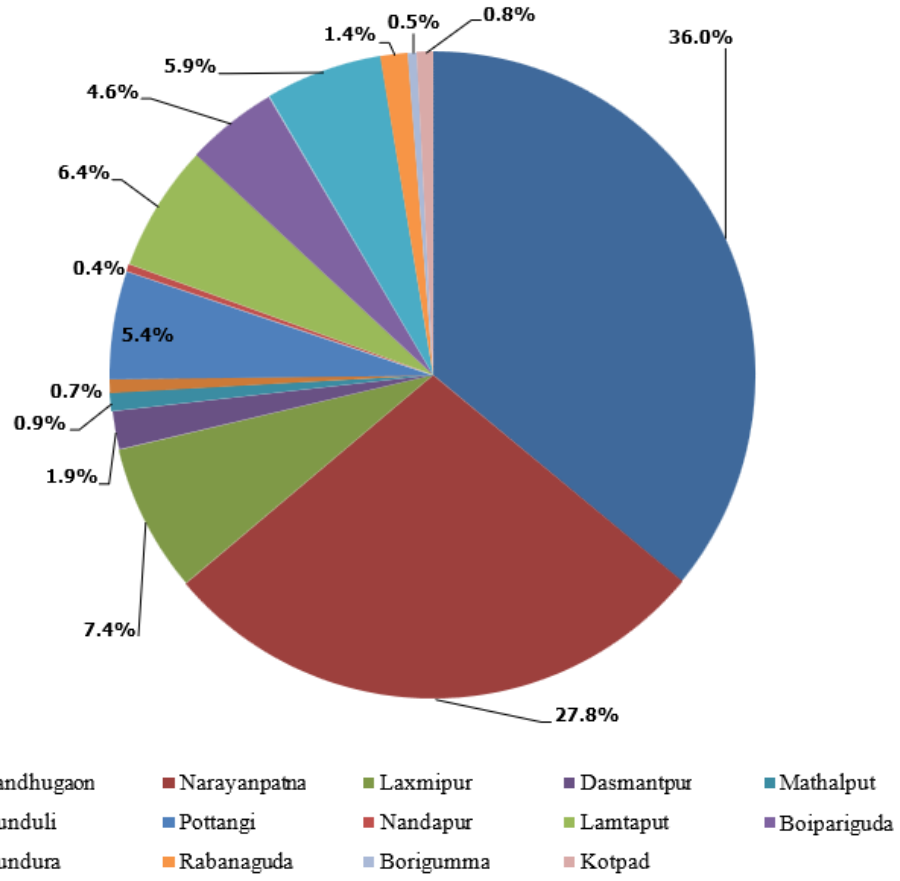

Figure 2: Percentage of API in different CHCs of Koraput district in 2020. (Source: CDMO Office, Koraput)

Narayanpatna CHC spans an area of about 726 sq. km with a population of 53015, of which 85.1% are tribes. There are 13 sub-centres (210 revenue villages) in this CHC. The distance between CHC and different villages ranges from 1-35 kms. Bandhugaon CHC is in contiguous to Andhra Pradesh in the east and Chhattisgarh to the western side spanning an area of 425 sq. km. The CHC comprises of 10 sub-centres (SCs) (166 villages) with a population of 68,698 predominantly constituted by several tribal communities (77%), the majority being Kondh (Table 2).

CHC	Area (sq.km)	No. of SCs.	No. of villages	No. of holdings	Population	No. of ASHAs
Bandhugaon	425	16	166	14584	68698	174
Narayanpatna	726	13	210	11321	53015	108

Table 2: Demographic details of the study CHCs.

Field survey

Malaria patients who were diagnosed and treated for P. falciparum infection with ACT (Artesunate with sulfadoxine and pyrimethamine) plus primaquine in these CHCs from January'22 to December'22 was eligible for the study. It was expected that; the patients would have consumed all the tablets present in the blister packets as per the instructions given by the health facility within 3 days. On the fourth day of post treatment, research team visited the patients' home and interviewed them using a semi-structured interview questionnaire which was designed for a face-to-face interview with the patient in the local language i.e., Odiya. Caregiver or head of the family was interviewed if the patient was below 17 years of age. Written informed consent was obtained for interviewing the participants. A written copy of the information was provided to the participants.

For considering the level of adherence (like following the drug consumption instructions by the drug supplier, elimination of parasites after treatment), the patients were sub-grouped into the following four categories

- Adhered to drug schedule and found negative for malaria parasite in microscopy and RDT.
- Adhered to drug schedule but found positive for malaria parasite in microscopy and RDT.
- Not adhered, if consumed all the tablets but did not follow the drug schedule.
- Certainly, non-adhered, if showing any remaining tablets.

Arrangements were made to treat him/her again to eliminate parasites from his/her blood for the patients who were found positive by RDT or microscopic testing. Patients who were found to have taken any treatment from traditional healers for malaria in addition to the treatment given by the CHC were also recorded. ITNs usage behaviour, maintenance practice and their perception on IRS were recorded by interviewing the head or any adult member of the 377 holdings from 115 randomly selected villages. Other information regarding demographic characteristics, socio-economic status, educational background, and geographical location of the patients were captured in a pre-designed data capture format.

The following information was collected from falciparum infected patients.

- Caregivers of the patients below 17 years were interviewed showing packets containing tablets.
- Whenever consumed ACT pack was available, pill count was done.
- The following factors were considered for determining the association with adherence and compliance to the ongoing intervention measures for malaria control.
- Patient factors- health seeking behavior
- Socio-economic status, demography
- Characteristics of therapy- vomiting
- Condition-related factors- clinical improvement
- Health system factors- communication of instructions
- Use rate of ITNs and acceptance to IRS in the community
- Acceptance of IRS

Patients who were positive either after adhering to the drug schedule or not adhered, were again advised to take treatment from their respective ASHAs were having advised to contact the concerned CHC for retreatment.

Sample size calculation

In total 400 falciparum infected malaria patients were included to estimate adherence to treatment. The sample size was determined with the assumption of percentage of treatment adherence is 50%, 5% of absolute precision and 95% confidence interval.

$$n = \frac{Z1-\propto/2p(1-p)}{d2}$$

Where, n is the sample size

$Z_{1-\propto/2}$ is the critical value of normal distribution

p is the percentage of adherence to treatment

d is the absolute precision

α is the level of significance

The patients' household was included to estimate the compliance to vector control intervention measures in the community.

Statistical analyses

Statistical analysis was carried out using logistic regression analysis to find out the risk factors of non-adherence to medicines and p-value < 0.05 was considered to be significant. All statistical analysis was done by STATA 14.2 (Texas, USA)

Results

Overall, 400 patients (218-Males and 182-Females) from 377 holdings were interviewed in 115 villages from both CHCs. 1653 members were present in 377 human dwelling. Out of the 400 patients interviewed, 232 (58.0%) patients were below 17 years of age. These 232 patients were present in 214 houses and the head of these houses were considered as caregivers and interviewed.

The age categories of the patients are furnished in table 3. Most of the surveyed houses (76.4%) were found to be made of mud walls with tiled roof/thatched roofs followed by reinforced cement concrete (RCC) buildings (19.1%), and cement walls with tiled roof/thatched roofs (4.5%).

Age category	No. of patients	%
<=5	58	14.5
6 – 18	195	48.8
19 – 40	112	28.0
>40	35	8.7
Total	400	100.0

Table 3: Age distribution of participants.

Details of Caregivers

The mean age (SD) of the caregivers was found to be 34.50 (6.01), ranging from 22 to 55 years. The majority of the caregivers (119;54.3%) were found to be looking after 2 children who were below 17 years of age (Table 4). Out of 219 caregivers 97.6% were ST followed by SC. (1.4%) and general (0.9%).

Caregiver	No. of respondents (%)
Relationship with child?	
Mother	18 (4.8)
Father	192 (50.9)
Others	9 (2.6)
What is your age?	
Mean (SD)	34.50 (6.01)
Min – Max	22 – 55
How many children (below the age of 17 years) do you look after?	
1 Child	73 (33.3)
2 Children	119 (54.3)
3 Children	15(6.9)
4 Children	11 (5.0)
5 Children	1 (0.5)

Table 4: Details of caregivers interviewed.

Respondents' knowledge on malaria

Responding to the question "how do people get malaria", 308 (81.7%) respondents out of 377 told, it was due to mosquito bites combined with other causes like unclean water/ stale food and bad air, while 61 (16.2%) respondents told it was solely due to mosquito bite, 59 (1.3%) respondents told was of unclean water and only 3 (0.8%) respondents told they had no idea. On their practice of using traditional medicines given by local healers (Disharis), only 3 (0.7%) persons said that they had used traditional medicine but subsequently they had also taken Government supply medicines from CHC and got cured. Only one patient said that he was not cured even after using antimalarials supplied by CHC. (Table 5).

Questionnaire	No. of respondents answered (%)
How do people get malaria?	
Unclean water	59 (1.3)
Mosquito bite/Bad air/Unclean water/Stale food	308 (81.7)
Mosquito bite	61(16.2)
No idea	3 (0.8)
Can malaria be cured by traditional medicines?	
Yes	1 (0.3)
No	240 (63.6)
Don't know	136 (36.1)
Have you taken traditional medicines to cure malaria?	
Yes	3 (0.7)
No	374 (99.3)
Have you got cured any time with government medicine?	
Yes	376 (99.8)
No	1 (0.2)
How serious do you consider malaria to be?	
Very serious	52 (13.7)
Serious	322 (85.4)
Not serious	3 (0.9)

Table 5: Respondents knowledge and practices on malaria

Treatment seeking behavior

All of 377 respondents said that they had asked the drug dispenser about drug schedule and 371 (98.4) persons out of them told that the drug dispenser had explained them as how to consume the medicines by showing them the blister pack. The other 6 respondents said that the drug dispenser had told them verbally, how to consume the tablets (Table 6).

Questionnaire	No. of respondents answered
Did you ask the drug dispenser, how to take medicines for malaria?	
Yes	377 (100.0)
No	-
If yes, how did he/she explain?	
Showed blister pack	371 (98.4)
Verbal instruction	6 (1.6)
Written instruction	-
Did you understand how to take medicines?	
Yes	377 (100.0)
No	-
Did you ask any doubts to the drug dispenser?	
Yes	374 (99.2)
No	3 (0.8)

Table 6: Treatment seeking behavior of the patients/caregivers

Adherence to ACT and PQ treatment

Out of the 400 patients surveyed 306 (76.5%) patients had adhered to the drug schedule. This was confirmed by the team by showing them the blister packets and asking them how they have consumed the tablets. Even 42 members showed the empty blister packets present with them.

Out of 94 non-adhered patients, 27 (28.7%) including caregivers of 10 patients below 17 years of age could not tell any reason, why they have not adhered to the drug schedule. Whereas, 2 (2.1%) patients told it was due to the bad taste of the tablets, 1(1.1%) patient said that it was because of the bigger size of the tablets, while 64 (68.1%) told it was because of a greater number of tablets (Table 7). When asked about the experience of any adverse effects of the drugs, out of 400 patients, 37 patients said that they had experienced vomiting, headache, and weakness after consuming the drugs.

Questionnaire	No. of respondents answered (%)
Did you feel any discomfort while taking the medicines regarding size of tablets?	
Yes	1 (1.1)
Did you feel any discomfort while taking the medicines regarding taste of tablets?	
Yes	2 (2.1)
Did you feel any discomfort while taking the medicines regarding number of tablets?	
Yes	64 (68.1)

Table 7: Response on "causes of non-adherence to 3 days ACT and PQ treatment"

When the research team asked the patients, possible reasons for non-consumption of the tablets by the villagers, 338 (89.6%) respondents said that they had no idea about this while 36 (9.5%) respondents said that this was due to a greater number of tablets, 1 (0.3%) respondent felt it was due to of adverse effects of the medicine, 1 (0.3%) respondent told, it was because of the size of the tablets and 1 (0.3%) respondent told it happened just because of negligence.

Compliance to vector control intervention measures

Insecticide Treated Net (ITNs)

ITN's were distributed twice in this area (2017 and 2020). The survey showed that a total of 989 LLINs were distributed to cover 1653 members of the surveyed 377 holdings (1.7 persons per net).

It was observed that 120 (31.8%) holdings had not used the net during the previous night of the surveyed day, whereas 257 (68.2%) holdings were using at least one of their received nets. When asked "why they are not using all of their received nets", 120 respondents could not give any answer (negligence). Twenty-six respondents told they have lack of space in their house to tie all of the received nets. Twenty-one respondents told some of their nets were damaged. Twelve respondents told they have washed the nets and are wet now. Nine respondents told they use mosquito repellents. Six respondents told they do not use it because of hot climatic conditions. One respondent said that he lost his net (Table 8).

Causes	No. of holdings
Net damaged	21
Using fan/repellant	9
Hot climate	6
Negligence	120
Net lost	1
No space in house	26
Washed	12

Table 8: Response of the respondents on keeping some of their LLINs without use.

While asking about the general habit of using LLINs, all of 377 respondents told that they do not use the LLINs regularly 191 (56.7%) respondents told they do not use the nets in hot/cold climates, 56 (16.6%) respondent did not answer anything (negligence) while 36 (10.7%) respondents told that their nets were damaged, 28 (8.3%) respondents told they use repellent/fan to avoid mosquito bites, 22 (6.5%) respondents told lack of space in their house to tie the nets, 3 (0.9%) respondents told the received nets are insufficient for their family while 1 (0.3%) respondent told he had experienced itching while using the net (Table 9).

Causes for irregular use (n=337)	No. of respondents answered (%)
Do not use in Summer/Winter	191 (56.7%)
Negligence	56 (16.6%)
Nets damaged	36 (10.7%)
Use repellent and fan to avoid mosquito bite	28 (8.3%)
Lack of space in their house	22 (6.5%)
Insufficient nets	3 (0.9%)
Itching while sleeping inside net	1 (0.3%)

Table 9: Response of the respondents on irregular use of LLIN.

Washing practices of LLINs

Out of 377 respondents, 370 (98.1%) told that they wash their LLINs in streams/ponds while 7 (1.9%) respondents told, they wash the LLINs in their home/near bore well. None of the holding members said that they washed their nets with warm or hot water. Only 15 respondents said that they dry their LLINs under shade after washing (Table 10).

Questionnaire	No. of respondents answered (%)
Where do you wash your nets?	
Stream/Pond	370 (98.1)
Home/bore well	7 (1.9)
If washing at home, which water you use?	
Cold water	377 (100.0)
Where do you dry your nets after washing?	
Outside under sun	362 (96.0)
Outside under shade	15 (4.0)
Do your village sprayed with DDT/other insecticide?	
Yes	121 (32.1)
No	102 (27.1)
Don't know	154 (40.8)
Have you allowed your house to get sprayed?	
Yes, partially	103 (27.3)
Yes, All rooms	6 (1.6)
Not got sprayed	268 (71.1)

Table 10: Response of the respondents on washing practices of LLINs and IRS in their villages

Compliance to Indoor Residual Spraying

When asked "whether your village has been sprayed with DDT", 102 (27.1%) heads of holdings answered "no" while 154 (40.8%) respondents said that they did not know whether their village had been sprayed or not, while 121 (32.1) respondents told, they knew when their village had been sprayed. Out of 121 participants who knew about the visit of the IRS spraying team to their village, only 6 (1.6%) told that they had allowed spraying in all rooms of their respective house, 103 (27.3%) allowed the spray team to partially spray in their house (leaving Puja room, Kitchen room, and food grain storage room) (Table 11).

Variable	Non-adherence		Unadjusted		Adjusted	
	Yes (n=94)	No (n=306)	OR (95% CI)	P-value	OR (95% CI)	P-value
Age						
>40	8(22.9%)	27(77.1%)	1.00	-		
18 – 40	23(17.3%)	110(82.7%)	0.71(0.28 – 1.75)	0.452		
<=17	63(27.2%)	169(72.8%)	1.26(0.54 – 2.91)	0.592		
Gender						
Female	50(27.5%)	132(72.5%)	1.00	-		
Male	44(20.2%)	174(79.8%)	0.67(0.42 – 1.06)	0.088		
Education						
>5th grade	54(22.4%)	187(77.6%)	1.00	-	-	
<=5th grade	40(25.2%)	119(74.8%)	1.16(0.73 – 1.86)	0.526		-
Household size						
<5	57(25.5%)	167(74.5%)	1.00	-		
>=5	37(21.0%)	139(79.0%)	0.78(0.49 – 1.25)	0.301		
How do people get malaria?						
Mosquito bite	90(23.1%)	300(76.9%)	1.00	-	-	-
Others	4(40.0%)	6(60.0%)	2.22(0.61 – 8.05)	0.224		
Can malaria be cured by traditional medicines?						
No	56(21.9%)	200(78.1%)	1.00	-	-	-
Yes/Don't know	38(26.4%)	106(73.6%)	1.28(0.80 – 2.06)	0.307		

Table 11: Univariate logistic regression model for non-adherence of ACT

Level of adherence

Level of adherence showed that 306 patients are adhered to drug schedule and found negative for malaria parasite in microscopy and RDT and 94 patients are certainly non-adhered, if showing any remaining tablets.

Factors associated with non-adherence to 3 days malaria treatment

The statistical analysis using logistic regression analysis to find out the risk factors of non-adherence to medicines indicate that factors like age, education, knowledge on malaria could not be attributed to adherence to drug schedule. Only experience of discomfort (P=<0.001) and experience of adverse effects were significant causes (P=<0.001) (Table 12).

Variable	Non-adherence		Adjusted	
	Yes (n=94)	No (n=306)	OR (95% CI)	P-value
Did you feel any discomfort while taking the medicines regarding number of tablets?				
No	30(9.0%)	303(91.0%)	1.00	-
Yes	64(95.5%)	3(4.5%)	144.67(42.06 – 497.65)	<0.001
Did you have any adverse effect after consumption of medicines?				
No	61(16.8%)	302(83.2%)	1.00	-
Yes	33(89.2%)	4(10.8%)	12.69(3.19 – 50.57)	<0.001

Table 12: Multiple logistic regression model for non-adherence of ACT

Discussion

The present study was conducted to assess the level of adherence to 3 days treatment of ACT+PQ for P. falciparum infection. Kristin Banek et al. (2014) in his critical review on the subject, suggests that ACT adherence levels varied substantially between the study populations and comparison between studies was challenging due to differences in study design, definitions, and methods used to measure adherence [12]. A similar study conducted in the Amazon region of Brazil to know the level of adherence for P. vivax treatment had reported 86.4% of the patients adhered and 9.6% of the patients were in "certainly non-adhered category that showed the remaining tablets after completion of drug schedule regimen [24]. The present study showed 76.5% of patients adhered to the instructions while 23.5% showed the remaining tablets. Those patients who have not shown the remaining tablets had followed the 3 days drug schedule as per instructions. In Ghana, 36.6% of the patients were observed to have adhered to the treatment instructions. Surprisingly, >90% of the respondents had agreed that ACTs they consumed had bad taste and felt unpleasant [11]. While we observed, a miniscule proportion (2.1%) of the respondent's experienced discomfort while consuming the ACTs in terms of unpleasant taste. This implies that with a robust and sustained IEC campaign, the perception of this miniscule proportion of individuals could be altered, paving way for completed compliance. This would pave way for elimination of malaria in the region and also prevent development of resistance to ACTs.

Alexandria et.al. (2015) documented reported 57.3% adherence to the ACT treatment and attributed it to patients' knowledge on the dosage, efficacy, and side effects of the ACTs used for the management of malaria, patients' awareness of the consequences of not completing the doses of antimalarial dispensed [3]. However, we did not observe any such condition. In the current study adherence level was assessed by enquiring about the number of days the tablets were consumed and observing the remaining tablets. The blister packets containing the ACT carried the instruction/guidance marks for day-wise consumption and also the age group for which the packet**,** is concerned to facilitate the patient/caregivers for its correct use. Similar findings were reported in a study carried out in public sector and found that ACT provided with pictorial instruction could have enhanced compliance and consumption of correct dosages at the right time [25].

Meta-analysis on poor adherence in children less than five years of age related to the lack of appropriate dose formulations for this vulnerable age group [25]. In the current study, 76.5% were adhering to the instructions and out of them 55.2% were below 17 years of age. This could be because of different colored blister packs for different age groups with the understandable day-wise marks for drug intake. The study had also reported that due to traditional beliefs and high costs of ACT, parents or caregivers of children could favor traditional medication over ACT [25].

Moreover, co-administration of ACT with traditional medication could lead to treatment interruption, sub-therapeutic drug concentration, sub-optimal parasitological and clinical response, and non-adherence [25]. On the contrary, in the present study, carried out in a predominantly tribal dominated area where tribal patients relay more on traditional approaches, only 0.25% of patients felt that where malaria could be cured with traditional medicine, while 0.7% of patients had taken traditional medicines from the local traditional healers along with ACT and PQ.

Studies on efficacy of ACT in malaria-endemic setting concluded that treating uncomplicated malaria with ACT showed greater efficacy in curing the disease, reducing transmission and producing a lower level of re-infection [26], reducing the average hospital stays and rapid clearance of parasites as compared to any other anti-malarial [27]. We observe of similar outcomes from the current study. All of the patients had consumed ACT supplied at the CHC and out of 94 who had not adhered, those who had even taken at least 25% of the supplied tablets were negative in RDT and microscopy. It was also observed that all of the patients had brought back the medicines to their homes without staying in the hospital. One of the important findings of the present study is that, the tribal patients preferred ACT to the traditional medicines a practice which is common among tribal communities (Figure 3).

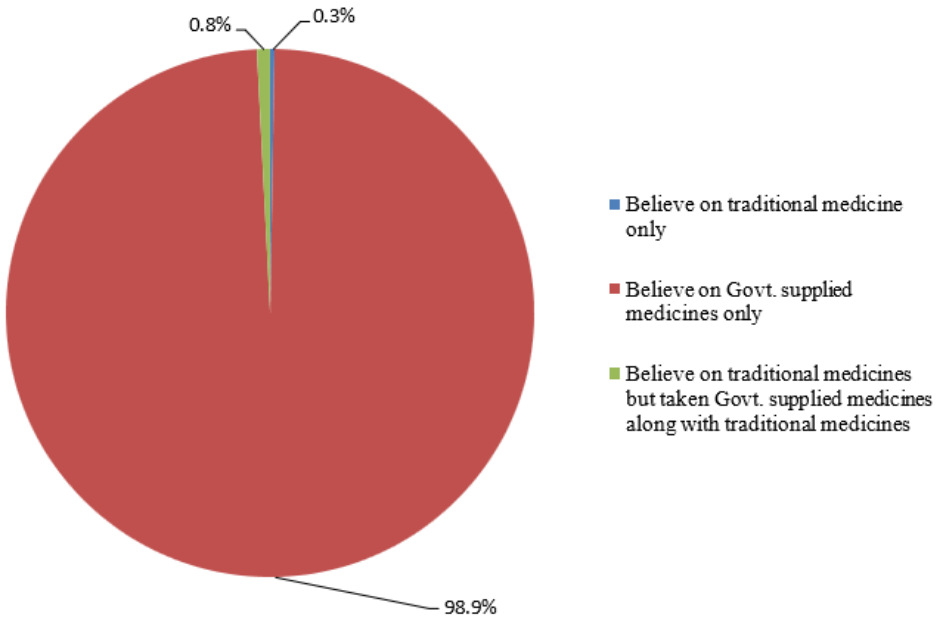

Figure 3: Treatment seeking behaviour of the participants

Conclusions

Non-adherence to malaria treatment would be participate in development of drug resistance. Non-adherence to ACT was primarily due to negligence of patients as after one or two days after consuming the medicines they were relieved from fever. The tribal patients preferred ACT over the traditional medicines for malaria treatment. In spite of the awareness that mosquito bites cause malaria, not using the LLINs poor maintenance and non-acceptance of IRS are most likely reasons for persistence of malaria in this area. People should be educated about the implications of poor adherence to ACT and at the same time they should be educated about the wastage of Government resources by not using the LLINs and non-acceptance to the IRS. Therefore, a robust information, education, and communication (IEC)/ behaviour change communication (BCC) mechanism should be in place such a mechanism not only could enhance the compliance to ACT but also facilitate in decreasing the malaria cases coupled by creating awareness on LLIN use and IRS acceptance. For the future, further in-depth studies on individual factors and barriers associated with non-adherence to ACT are needed, to make informed policy choices and improve the drug delivery system for effective malaria treatment which would hasten the process and elimination of malaria.

List of abbreviations

ACT - Artemisinin-based combination therapy
ASHAs - Accredited Social Health Activists
CHC - Community Health Centre
ITNs - Insecticide treated nets
IRS - Indoor residual spraying
CQ - Chloroquine
PQ - Primaquine
WHO - World Health Organization
AL - Artemether-lumefantrine
AS-AQ - Artesunate-amodiaquine
AS-MQ - Artesunate-mefloquine
AS-PND - Artesunate-pyronaridine
AS-SP - Artesunate-sulfadoxine/pyrimethamine
PQ - primaquine
DHA-PPQ - Dihydroartemisinin-piperaquine
NCVBDC - National Centre for Vector Borne Disease Control
ASHA - Accredited Social Health Activists
ICMR-VCRC - Indian Council of Medical Research-Vector Control Research Centre
CDMO - Chief District Medical Officer
RDT - Rapid Diagnostic test

IHEC - Institutional Human Ethical Committee
RCC - Reinforced Cement Concrete
SD - Standard Deviation
SCs - Sub-centres
DDT - Dichlorodiphenyltrichloroethane
VBDTS - Vector Borne Disease Technical Supervisor
LT - Laboratory technician
IEC - Information, Education, and Communication
BCC - Behaviour change communication

Declarations

Ethics approval and consent to participate:

Ethical permission for the research was sought and granted by the Institutional Human Ethical Committee (IHEC), ICMR-VCRC, Pondicherry. (IHEC-0421/N/N). Consent from all of the participants of this study was obtained at the time of survey.

Consent for publication:

All the authors involved in the study have given their consent to publish the manuscript.

Availability of data and materials:

Relevant data was obtained from the CHCs are available within the manuscript in the form of primary tables and graphs. Data is available on reasonable request to ICMR-VCRC.

Competing interests:

The authors declare that they have no competing interests

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Authors' contributions

DKP, ANS, AK Conceptualized the study design. DKP, MMB supervised the conduct of study. DKP & VK performed the curation of data and statistical analysis. DKP & ANS drafted and edited the original manuscript; AK critically reviewed the manuscript. All authors read and approved the final version of the manuscript.

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