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Received: 26 June 2024

Accepted: 20 August 2025

Published: 26 September 2025

Citation:

Lee TT, Omoluabi E, Ayodeji K,
Yusuf O, Okon C, Brunner NC,
Delvento G, Signorell A, Lambiris MJ,
Kwiatkowski M, Burri C, Lengeler C,
Emedo E, Cheshi F, Fashanu C,
Wiwa O and Hetzel MW (2025)
Treatment-Seeking for Children with
Suspected Severe Malaria Attending
Community Health Workers and
Primary Health Centres in Adamawa
State, Nigeria.
Int. J. Public Health 70:1607697.
doi: 10.3389/ijph.2025.1607697

Treatment-Seeking for Children with Suspected Severe Malaria Attending Community Health Workers and Primary Health Centres in Adamawa State, Nigeria

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Objectives: In the context of introducing pre-referral rectal artesunate for children with severe malaria in Adamawa State, Nigeria, case fatality was 19% among severely sick children visiting primary health centres (PHCs), and 6% among those visiting community health workers (CORPs). To understand this difference, we investigated illness severity, treatment-seeking, and background characteristics of these patients.

Methods: 589 children <5 years of age with fever and danger signs indicative of severe malaria attending CORPs (N = 314) and PHCs (N = 275) were enrolled. After 28 days, caregivers were interviewed about background characteristics, symptom severity, and treatment seeking practices; children attending CORPs and PHCs were compared.

Results: Compared to children attending CORPs, those attending PHCs were more likely to live in urban areas, have ≥4 clinical danger signs (50% vs. 39%, p = 0.02) and signs of central nervous system involvement (90% vs. 74%, p < 0.01), and more often received initial home treatment (42% vs. 33%, p = 0.04).

Conclusion: PHCs may see sicker children due to community assumptions of their professional capacity. Health system strengthening is required to capacitate PHCs to handle severe conditions and save lives in rural communities.

Keywords: case fatality, primary health care, severe febrile illness, malaria, quality of care

Abbreviations: ACT, Artemisinin-based Combination Therapy; AOR, Adjusted Odds Ratio; CARAMAL, Community Access to Rectal Artesunate for Malaria; CFR, Case Fatality Rate; CNS, Central Nervous System; CORP, Community Oriented Resource Person; iCCM, integrated Community Case Management; IMCI, Integrated Management of Childhood Illnesses; LGA, Local Government Areas; mRDT, malaria Rapid Diagnostic Test; PHC, Primary Health Center; RAS, Rectal Artesunate; WHO, World Health Organization.

INTRODUCTION

Nigeria accounts for 26% of the world's malaria cases and 31% of malaria deaths [1]. The country is challenged with high levels of poverty, a large rural population with few transportation options, and a generally poorly functioning health system, particularly at the rural primary care level [2].

Uncomplicated malaria may progress to severe disease and death if it is not appropriately treated [3–5]. This process can occur quickly; therefore, early diagnosis and prompt, effective management are essential [6]. Initial malaria treatment is generally provided by primary health centres (PHC) and, in several countries in sub-Saharan Africa and beyond, by community health workers [7]. In Nigeria, community health workers, known as Community Oriented Resource Persons (CORPs), implement the integrated community case management (iCCM) guidelines and primary health centers (PHCs) implement the integrated management of childhood illnesses (IMCI) algorithm. Both, CORPs and PHCs serve as first point-of-care; for severe conditions, both providers are supposed to refer children directly to a hospital. According to guidelines, both of these providers treat children with uncomplicated malaria with oral artemisinin-based combination therapy (ACT), while children with suspected severe malaria are referred to health facilities with inpatient departments for comprehensive clinical management [6]. Referral facilities are few and often more difficult to access, particularly from remote rural areas.

In an observational study, the Community Access to Rectal Artesunate for Malaria (CARAMAL) project investigated the introduction of rectal artesunate (RAS) as pre-referral treatment for children with suspected severe malaria in Nigeria, the Democratic Republic of the Congo, and Uganda [8]. RAS products were recently pre-qualified by WHO [9], several years after a clinical trial found pre-referral RAS to reduce death or permanent disability when administered to children under the age of 6 years with suspected severe malaria who delayed referral to a higher level health facility [10]. In Nigeria, the CARAMAL study did not find a positive health effect of introducing pre-referral RAS in three Local Government Areas (LGA) of Adamawa State. The study also found that the case fatality rate (CFR) among children reporting with signs of severe malaria was higher in children attending a PHC (18.5%) compared to those attending a CORP (5.7%) [9].

Mortality from malaria is affected by several factors, including the *Plasmodium* species, transmission intensity and vector control measures, age and health status of a person, and the effectiveness of antimalarial treatment [11, 12]. In the context of introducing pre-referral RAS in Nigeria, this study focused on the latter two aspects. The severity of a child's condition, approximated by the presence of clinical danger signs or caregiver's perceptions, may determine and explain treatment seeking [13]. Conversely, prompt treatment seeking is also critical to prevent progression to severe disease and death [12]. In Nigeria, among children who sought professional care for fever, only 68% did so within 24 h of illness onset [14] and home treatments for malaria are reported to be poor [15]. Costs

and distance to a health facility are barriers to pursuing appropriate treatment [16, 17].

While a prompt visit to a community-based provider, such as a CORP or PHC, can accelerate treatment initiation for common conditions, severely ill patients may need to be referred to a higher level provider for appropriate care. In the CARAMAL project, two critical aspects of a functioning continuum of care for severe malaria cases, namely referral completion and post-referral treatment, were often not implemented according to guidelines, as described elsewhere [18, 19]. However, neither of these system shortfalls seem to provide an explanation for the difference in CFR between the two groups of patients [9].

Understanding reasons for the differences in CFR between children who visited CORPs and those who visited PHCs as community level providers is crucial to strengthen primary healthcare and reduce child deaths. We investigate patients enrolled in the CARAMAL project, focusing on the type and severity of symptoms, home treatment and treatment seeking delay, while taking into account background characteristics of the patients.

METHODS

Study Design

This investigation was part of the CARAMAL project, an observational study that accompanied the roll-out of pre-referral RAS into existing iCCM and IMCI systems, as detailed elsewhere [8]. This analysis includes a cohort of children with suspected severe malaria who were prospectively enrolled by community-based providers (CORPs or PHCs) in Nigeria and followed-up at their household 28 days after enrolment.

Setting

Study sites were Fufore, Mayo-Belwa and Song Local Government Areas (LGAs) of Adamawa State in northeastern Nigeria. The estimated total population of these LGAs was 746,950 in 2018, of which 130,430 (17%) were under the age of 5 years [20]. The population in the three LGAs is served by over 500 CORPs, 77 PHCs, and 3 referral health facilities (Cottage Hospitals). In the study area, malaria occurs seasonally.

CORPs and PHCs provide community-level primary healthcare services. The PHCs are usually small facilities with nurses, midwives and lower cadre staff. In contrast, CORPs are commonly not health professionals but lay persons in the community with a minimal training in basic healthcare provision. CORPs obtain medical supplies and supervision from nearby PHCs or NGOs. CORPs were introduced by the local health authorities in 2014 to fill an accessibility gap and serve hard to reach communities more than 5 km away from a health facility.

Data Collection

Children under 5 years identified as cases of "severe malaria" at a PHC, or visiting a CORP with a history of fever and at least one general danger sign indicative of suspected severe malaria according to Nigerian iCCM guidelines (unusually sleepy or

unconscious, not able to drink or feed, vomiting everything, convulsions, or yellow eyes), were enrolled between June 2018 and July 2020. A malaria rapid diagnostic test (mRDT) was conducted for study purposes. CARAMAL staff attempted to reach both types of providers weekly by phone to identify and register children meeting the inclusion criteria. Follow-up visits were done 28 days later in-person at the child's residence, or by phone during the COVID-19 pandemic lockdown. Caregiver interviews were conducted in the local language (Hausa or Fulfulde) about the child's health status, signs and symptoms of disease, treatment seeking perceptions and practices, and medicines the child received. Geo-locations of the child's home were recorded. Children who died were followed up 2 to 3 months after enrolment to respect the mourning period. Additional details about the circumstances of the death were recorded. Data was collected electronically on password protected tablets using ODK Collect, and saved on a secure ODK Aggregate server hosted at the Swiss Tropical and Public Health Institute in Switzerland.

Data Analysis

Study participants were included in the analysis if they fulfilled all inclusion criteria including at least one iCCM danger sign and a positive mRDT at enrolment, a successful follow-up on day 28, and written consent provided by their caregiver. Children who died more than 31 days after enrolment were excluded from the analysis.

This study compares children attending a CORP with children attending a PHC. The main variables of interest were home treatment, treatment seeking delay, presence of danger signs and reasons for attending the CORP or the PHC. Home treatment was coded as a categorical variable. Treatment seeking delay was defined as the reported number of days between illness onset and attending the CORP or PHC, categorized into two-day periods. We used the presence of danger signs involving the central nervous system (convulsions, unusually sleepy or unconscious), number of danger signs (both general iCCM danger signs used as part of the inclusion criteria and other Nigeria-specific danger signs), and caregiver-perceived severity as proxies for disease severity. Danger signs were consolidated from health worker reports at enrolment and caregiver information at day 28. Binary variables were derived to account for key time periods that may have influenced outcomes: the RAS roll-out period (starting in May 2019), the COVID-19 movement restriction period (1st April 2020 to the end of study in July 2020), and the rainy season (May to October). Living in a rural or urban setting was determined based on the child's residence geo-location and the LandScan HD: Nigeria version 1.1 geodatabase (Oak Ridge National Laboratory, 2018) settlement patterns defined by Weber et al. [21].

Descriptive analyses investigated differences between patients attending a CORP versus those attending a PHC. Logistic regression models with clustered standard errors (clustering at the level of the enrolling healthcare provider) were adjusted for the COVID-19 pandemic lockdown period that was likely to affect treatment seeking. Clustered standard errors were used

because cluster membership determines outcome [22]. P-values were calculated using the likelihood ratio test for categorical variables and on the odds ratio for binary variables. P-values of <0.05 were considered statistically significant. Unadjusted models are presented as supplementary materials. Statistical analyses were conducted in Stata SE version 16.1.

RESULTS

Study Population

CORPs and PHCs provisionally enrolled 724 children. Of those, 66 (9%) were lost to follow-up or the caregiver did not provide consent and 33 (5%) did not fulfill the inclusion criteria (7 had no history of fever, 26 no danger sign at enrolment). Two children who died >31 days after enrolment were excluded, as well as 34 who had no positive mRDT at enrolment (**Supplementary Figure S1**).

The final analysis included 589 children with suspected severe malaria, of which 314 (53%) attended a CORP and 275 (47%) a PHC (**Table 1**). They were enrolled at 139 different providers (108 CORPs, 31 PHCs). CORPs enrolled fewer patients per provider (median: 1, IQR: 1–2, range: 1–38) compared to PHCs (median: 5, IQR: 1–12, range: 1–42).

Patient Characteristics

Overall, there were more male ($n = 352$) than female ($n = 237$) patients in the study and the mean patient age was 2.0 years. Caregivers were mostly female and between 25 and 34 years old. More children were enrolled in the rainy season ($n = 440$) than the dry season ($n = 149$). There were no differences in the aforementioned aspects between patients enrolled by CORPs and PHCs (**Table 1**, unadjusted estimates **Supplementary Table S1**). Children attending PHCs were more likely to live in an urban area (adjusted odds ratio [AOR]: 4.6, 95% CI: 1.4–15.4) and less likely to visit the facility during a weekend (AOR: 0.5, 95% CI: 0.3–0.9). They were also more often enrolled after the introduction of RAS in the study area than before (AOR: 3.3, 95% CI: 1.7–6.4), and during the COVID-19 pandemic (AOR: 1.9, 95% CI: 1.0–3.6) that occurred after the introduction of RAS.

Signs and Symptoms

Convulsions (79%) and being unusually sleepy or unconscious (70%) were more common in children visiting a PHC (**Figure 1**). Together, these symptoms involving the Central Nervous System (CNS) were reported more frequently in children visiting a PHC (90%) than in children visiting a CORP (74%) (AOR: 3.5, 95% CI: 1.9–6.1). There was no significant difference in the proportion of children with CNS symptoms during the COVID-19 pandemic (79%) compared to prior to the pandemic (82%).

Children enrolled at CORPs were more often reported to vomit everything (72%) or be unable to drink or feed anything (64%). Vomiting everything, prolonged fever (≥ 7 days) and blood in the stool were reported significantly more frequently among children attending a CORP (**Figure 1**).

Children often presented with multiple symptoms. More children attending a PHC (50%) had ≥ 4 danger signs

TABLE 1 | Patient characteristics by type of provider visited (Adamawa State, Nigeria, 2018–2020).

	CORP		PHC		AOR ^a	95% CI ^a	p-value ^a
	N	%	N	%			
Total	314		275				
Child sex							
Male	188	60	164	60	Ref.		
Female	126	40	111	40	1.0	(0.7–1.3)	0.91
Child age (years)							
0	40	13	27	10	Ref.		0.34
1	86	27	74	27	1.3	(0.7–2.6)	
2	82	26	82	30	1.5	(0.8–2.9)	
3	68	22	55	20	1.3	(0.6–2.4)	
4	38	12	37	13	1.5	(0.7–3.4)	
Caregiver sex							
Male	102	32	95	35	Ref.		
Female	212	68	180	65	0.9	(0.6–1.3)	0.48
Caregiver age							
<25	42	13	46	17	Ref.		0.17
25–34	167	53	128	47	0.7	(0.4–1.2)	
35–45	75	24	72	26	0.8	(0.5–1.5)	
>45	30	10	28	10	0.9	(0.4–1.7)	
Missing	0	0	1	0	-		
Caregiver education ^b							
Never attended school	54	17	65	24	Ref.		0.77
Primary or lower	15	5	26	9	1.5	(0.6–3.4)	
Secondary or higher	28	9	44	16	1.3	(0.6–2.6)	
Quranic	22	7	39	14	1.5	(0.7–3.1)	
Missing	195	62	101	37	-		
LGA							
Fufore	143	46	94	34	Ref.		0.02
Mayo-Belwa	95	30	154	56	2.3	(0.5–10.4)	
Song	76	24	27	10	0.5	(0.1–1.9)	
Residence							
Rural	298	95	227	83	Ref.		
Urban	14	4	43	16	4.6	(1.4–15.4)	0.01
Missing	2	1	5	2	-		
Day of enrolment							
Workday	241	77	239	87	Ref.		
Weekend	73	23	36	13	0.5	(0.3–0.9)	0.02
Season							
Dry season	83	26	66	24	Ref.		
Rainy season	231	74	209	76	1.0	(0.6–1.6)	0.95
RAS implementation phase							
Pre-RAS	156	50	61	22	Ref.		
Post-RAS	158	50	214	78	3.3	(1.7–6.4)	<0.01
COVID-19 pandemic							
Pre-COVID-19	268	85	207	75	Ref.		
COVID-19 period	46	15	68	25	1.9	(1.0–3.6)	0.04

^aLogistic regression adjusting for the COVID-19 pandemic period, with standard errors clustered at the level of the health care provider. Likelihood ratio test used to calculate p-values for categorical variables.

^bData not collected during the entire study period.

compared to children attending a CORP (39%) ($p = 0.02$) (Table 2, unadjusted estimates Supplementary Table S2). Three-quarters of caregivers perceived their child's illness to be serious but not fatal, with no statistically significant difference between the two compared groups.

Home Treatment

Treatment provided at home prior to attending a healthcare provider was more common among patients attending a PHC

than those attending a CORP (CORP: 33%, PHC: 42%) (Table 3, unadjusted estimates Supplementary Table S3). Treatments included modern medicines, traditional medicines or herbs, and washing or sponging to cool the fever. Caregivers who were able to name the medicine provided prior to attending a health provider most often mentioned paracetamol (CORP: 85%, PHC: 92%) and occasionally the first-line antimalarial artemether-lumefantrine (CORP: 15%, PHC: 14%). The type of home treatment did not differ between the two groups.

Treatment Seeking

Further treatment seeking details were analysed for 264 children who attended a CORP and 242 who attended a PHC. There was no substantial difference in the number of days between illness onset and visiting a CORP or a PHC (Figure 2A). Among children attending a CORP, 38% attended the same day or the day after illness onset and 32% 2–3 days after becoming ill. Among PHC enrolments, slightly more children attended the PHC 2–3 days after symptom onset (41%) compared to the same day or day after (35%). Home treatment was associated with a longer treatment seeking delay. Children for whom prompt care was sought had the lowest rates of home treatment administration (CORP: 18% and PHC: 32%) compared to those with delays greater than 1 day (CORP: 44% and PHC: 52%; $p < 0.01$). Before visiting the enrolling CORP or PHC, 14% of children attending a PHC and 8% of those attending a CORP had been to another provider (AOR: 2.2, 95% CI: 1.1–4.4). In most cases, the previous provider was a chemist/pharmacy/drug shop for both CORP (47%, 9/19) and PHC (71%, 24/34) enrolments (Fisher's test $p = 0.85$). The COVID-19 pandemic was found to decrease the proportion seeking timely treatment (same or following day) from CORPs (AOR: 5.1, 95% CI: 1.8–14.3) but not from PHCs (AOR: 1.5, 95% CI: 0.7–3.1).

PHCs, offering a wider range of services and being much fewer than CORPs, were significantly more likely to be located outside the child's locality than CORPs (50% vs. 6%; AOR: 18.0, 95% CI: 6.8–47.2) (Figure 2B).

A total of 456 caregivers provided reasons for taking their child to a CORP or a PHC (Figure 3). The most common reasons for visiting a CORP were knowing (76%) and trusting (26%) the health worker and low cost (22%). In contrast, reasons for attending a PHC included the experience (49%) and medical professionalism (34%) of PHC health workers, as well as knowing the facility (32%). Knowing or trusting the provider and the service being inexpensive were significantly more common among caregivers who brought their child to a CORP, whereas experience and professionalism of the provider and an expectation or custom to consult this provider were more frequent reasons for attending a PHC.

DISCUSSION

Severely sick children need prompt diagnosis and effective clinical management to prevent long-lasting sequelae or death [6]. Diagnostic algorithms such as iCCM and IMCI should allow rapid triaging of severely sick patients close to a patient's home,

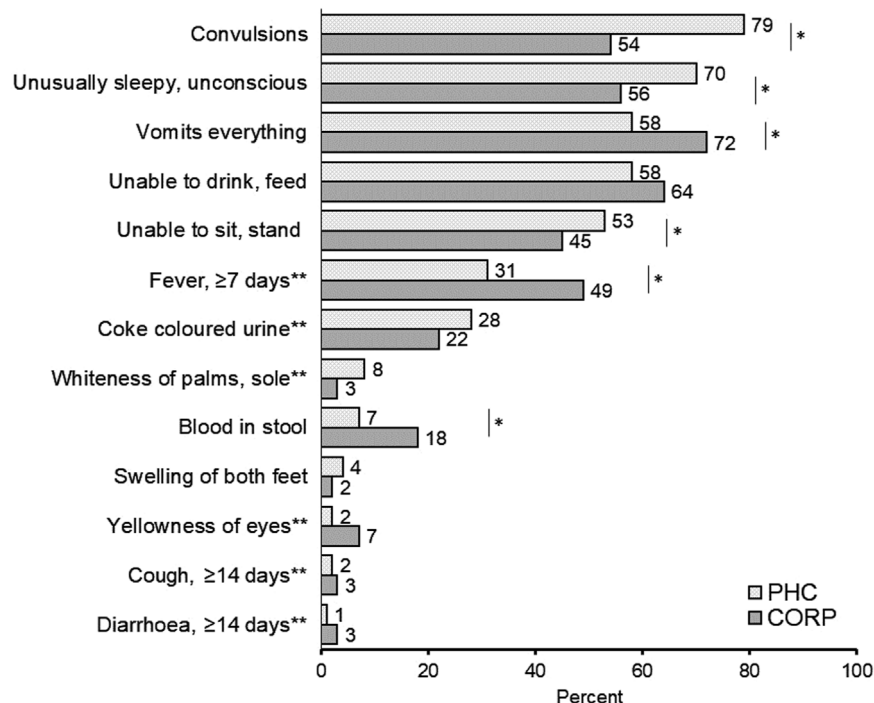


FIGURE 1 | Signs and symptoms of severity during the child's case of severe illness stratified by community-based health provider visited (Adamawa State, Nigeria, 2018–2020). * $p < 0.05$. **Data not collected during the entire study period.

TABLE 2 | Number of danger signs and caregiver's perceived severity of the illness (Adamawa State, Nigeria, 2018–2020).

	CORP		PHC		AOR ^a	95% CI ^a	p-value ^a
	N	%	N	%			
Total	314		275				
Number of danger signs ^c							
0–1 ^b	52	17	32	12	Ref.		0.02
2–3	138	44	106	39	1.4	(0.8–2.4)	
≥4	124	39	137	50	2.0	(1.2–3.4)	
Perceived severity of the illness							
Not fatal	236	75	193	70	Ref.		
Fatal	76	24	79	29	1.3	(0.8–2.0)	0.25
Don't know/missing	2	1	3	1	-		

^aLogistic regression adjusting for the COVID-19 pandemic, with standard errors clustered at the level of the health care provider. Likelihood ratio test used to calculate p-values for categorical variables.

^b3 children were not said to have any danger signs by caregivers at follow-up but health providers noted danger signs at enrolment.

^cOnly includes danger signs collected across the whole study period.

TABLE 3 | Actions taken at home prior to consulting health providers (Adamawa State, Nigeria, 2018–2020).

	CORP		PHC		AOR ^a	95% CI ^a	p-value ^a
	N	%	N	%			
Total	314		275				
Any home treatment							
No	209	67	157	57	Ref.		
Yes	103	33	116	42	1.5	(1.0–2.1)	0.04
Missing	2	1	2	1	-		
Actions taken	103 ^b		116 ^b				
Traditional medicines/herbs	22	21	26	22	1.1	(0.5–2.2)	0.86
Tepid sponging	7	7	17	15	2.4	(0.9–6.4)	0.09
Modern medicine	79	77	85	73	0.8	(0.5–1.5)	0.55
Medicines given (if known)	67 ^b		76 ^b				
Artemether-lumefantrine	10	15	11	14	1.0	(0.3–3.2)	0.99
Oral rehydration solution (ORS)	1	1	1	1	0.8	(0.1–13.4)	0.89
Paracetamol	57	85	70	92	2.1	(0.6–7.0)	0.23
Other	6	9	5	7	0.7	(0.2–2.5)	0.56

^aLogistic regression adjusting for the COVID-19 pandemic, with standard errors clustered at the level of the health care provider.

^bDenominator for this variable.

and ensure administration of pre-referral treatment and transfer to a higher-level health facility. In Nigeria's Adamawa State, we found that children with suspected severe malaria who attended a PHC were three times more likely to die than those who visited a CORP (CFR 18.5% vs. 5.7%, [9]), a finding that could not be explained by differences in referral delay or post-referral

antimalarial treatment [9]. We therefore investigated differences in background characteristics and treatment history of patients who attended a CORP or a PHC, respectively, to better understand the observed difference in CFR.

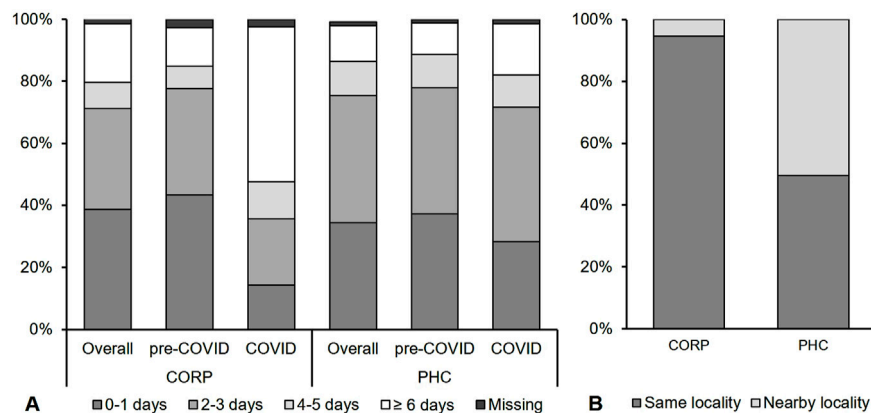


FIGURE 2 | Treatment seeking at community-based providers: **(A)** Time between illness onset and visiting the respective provider in days by enrolment period; **(B)** Location of the enrolling provider in relation to the child's residence (Adamawa State, Nigeria. 2018–2020).

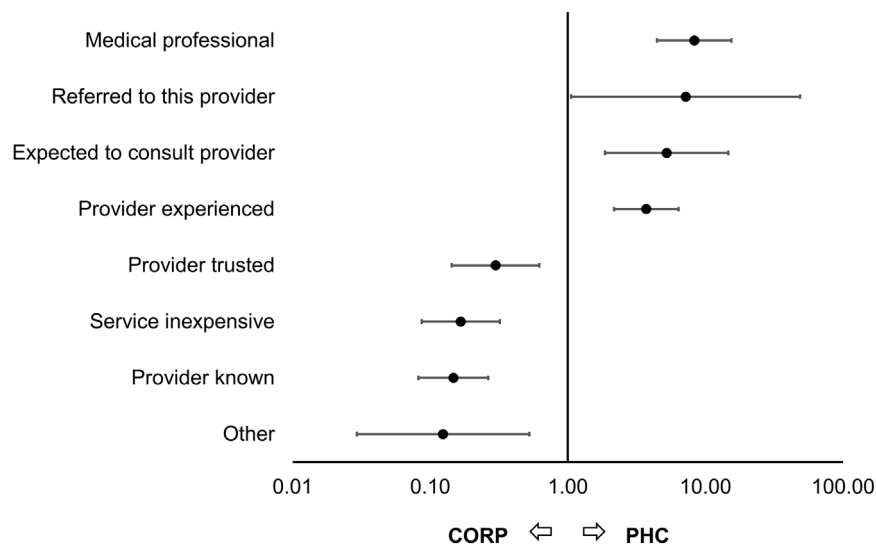


FIGURE 3 | Odds ratios for reasons caregivers took their child with severe febrile illness to a Primary Health Centre (PHC) compared to a Community Oriented Resource Person (CORP) (Adamawa State, Nigeria. 2018–2020). Logistic regression adjusting for the COVID-19 pandemic, with standard errors clustered at the level of the healthcare provider.

There were no significant differences in demographic characteristics of patients attending CORPs or PHCs. However, those attending PHCs lived in more urban areas, which may reflect socio-demographic differences not directly visible in our data. Children at PHCs also appeared to be more severely ill as reflected in the presence of CNS danger signs (90% vs. 74% in those attending CORPs). As the observational study design did not allow for an expert clinical examination, the presence of CNS symptoms was used as a proxy for severe disease, as previously done in similar situations [23–26]. Severity was also reflected in more children attending a PHC having ≥ 4 clinical danger signs compared to children

taken to a CORP. While this analysis considered danger signs on which CORPs were specifically trained, the more thorough clinical training of health workers at PHCs may have biased the recognition of danger signs. Yet, while danger signs indicated that more severely ill children were rather brought to a PHC, this was not reflected in higher caregiver-perceived illness severity, though this study did not explore multidimensional aspects of perceived severity (e.g. emotions, knowledge about severe malaria, economic consequences in seeking or not seeking treatment) [13].

It is plausible that more children with specific signs of severity are rather brought to a PHC than to a CORP as caregivers assume

higher professionalism and experience of providers at PHCs. Greater illness severity increased the likelihood of care seeking at health centres compared to community-health workers and self-care in Papua New Guinea [17]. Warsame et al. (2016) previously found that children attending community health workers, in settings comparable to ours, had higher rates of CNS symptoms compared to those attending other health providers such as trained mothers or traditional healers, suggesting higher perceived professional capacity [26]. In Burkina Faso, cases of severe disease often bypass community health workers in favour of a professional health worker [27]. CNS symptoms and difficulties in breathing as signs of severity in febrile children have also been associated with hospital attendance in rural Tanzania [28].

Initial home treatment (usually an antipyretic, rarely an antimalarial) and first attending another provider (mostly a drug shop/chemist/pharmacy) were more common among children brought to a PHC compared to those brought to a CORP. This pattern may reflect a staged escalation in the level of care if symptoms do not improve. As observed elsewhere [29], and also in our study, home treatment and attending medicine retailers did not facilitate access to appropriate medicines but more likely delayed the administration of appropriate treatment by a qualified healthcare provider. As a result, an uncomplicated malaria episode may have progressed to severe malaria, or urgent treatment of an already severe illness episode may have been delayed. In Nigeria, lower quality providers are more often sought for children of lower socioeconomic status [30–32] and most drug sellers are not integrated in the formal health system and the continuum of care for severe malaria (for instance, they do not administer pre-referral RAS).

Two-thirds of the children in our study were not brought to the PHC or CORP on the day of onset of symptoms or the day after. Whether delay in attending a healthcare provider has contributed to the overall high CFR in Adamawa is unclear since we lack information on how quickly a particular episode became severe. Yet, it is known that treatment seeking delays increase the risk of progressing from uncomplicated to severe malaria [33] and mortality is highest within 24 h of onset of severe disease [12]. Distance and transport time may negatively affect the condition of a severely sick child especially if transport is strenuous. In Zambia, greater distance from the hospital increased the odds of death in children with severe malaria [34].

We did not find a significant difference in treatment seeking delay between children attending a CORP or PHC, though the retrospective assessment with a 28 days recall period may have limited how precisely time periods were recalled. Thus, some nuances in treatment delay may have remained undetected. During COVID-19 pandemic movement restrictions, delay in seeking treatment increased substantially among those going to a CORP but only marginally among those attending a PHC. CORPs experienced stockouts of commodities and delay in replenishment during the COVID-19 lockdown (own observations), which could have discouraged attendance. Additionally, over the course of the study, behavioural change

communication campaigns were conducted alongside RAS roll-out to sensitize communities [35] and may have contributed to caregivers' awareness about severe malaria and perception about health providers' capabilities in treating their child's illness.

Other factors may have influenced the choice of community-based providers without necessarily affecting the CFR. This includes the distance between a patient's home and the nearest CORPs, PHCs, and referral facilities, as well as the distance of these health providers to one another. Druetz et al. showed that in rural Burkina Faso, consulting a community health worker for malaria was associated with increased distance to the nearest health facility [36]. Provider operating hours also affect health-seeking behaviours. We found that on weekends, patients rather attended CORPs than PHCs that did not provide 24-hour service. A different finding was published by Koce et al. who found that in Nigeria, the limited staff and operating hours of community-based providers (compared to referral facilities) resulted in patients directly seeking care from hospitals, which usually operate 24 h and have medical doctors [37].

Taken together, our findings suggest that, compared to those attending a CORP, children who attended a PHC may have been more severely ill, potentially aggravated by inadequate home management, delay in attending the health facility, and possibly a longer and more strenuous travel. As recognition of malaria and severe disease is often poor [38], caregivers may have underestimated the severity of the child's condition even in the presence of danger signs. Combined with a low capacity of PHCs to manage severe illness, these factors may have contributed to a higher CFR among children attending a PHC; however, they are unlikely to be the only explanation. Other factors affecting the health outcome of children in this study were investigated in separate analyses. For example, the likelihood of death was higher among children who were treated with pre-referral RAS (AOR: 2.42, 95% CI: 1.25–4.70), whereas a higher proportion of children attending PHCs received RAS compared to those attending CORPs [9]. This finding may be related to incomplete referral and the quality of post-referral care rather than to the administration of RAS itself. For example, only 48% of children completed referral to a Cottage Hospital after administration of RAS by a CORP or PHC, though children attending a PHC were much more likely to complete referral [18]. While hospitalized, injectable antimalarial treatment was common but <4% of children were subsequently treated with the required oral ACT [19]. Several suspected viral outbreaks occurred in Adamawa State during the study period, including Lassa Fever and Yellow Fever [39, 40]. The symptoms of these diseases are often unspecific and overlap with severe malaria, while health providers at all levels in remote locations often lack diagnostic capacity for these infections [41]. Over-diagnosis of severe malaria in children with severe febrile illness is also a well-known issue [42, 43]. While all children included in this analysis had a positive malaria RDT, severe illness and eventually death may have resulted from a missed or inappropriately managed co-infection. Further support for this is that the time between visiting the community-based provider and death was 6.3 days in Nigeria [9], however, the risk of death due to severe malaria is highest

early on. Our findings hence indicate that children in Adamawa State with a severe febrile illness indicative of severe malaria face a high risk of dying even if they attend formal primary healthcare services. Several factors along the continuum of care are likely to contribute to the high proportion of deaths in children attending a PHC, including the inadequate quality of treatment received at higher level referral facilities.

In the broader context, these findings underscore the necessity to not only improve access to primary healthcare services and prompt treatment initiation, but to implement health systems strengthening measures to improve referral systems and quality of care at all levels [44]. These considerations, based on findings in this publication and others emerging from the CARAMAL project, were presented at a technical consultation convened by the WHO with the aim to develop operational guidance for an effective implementation of pre-referral RAS in community-based health systems [45].

This study contributes to literature on care seeking for severely ill children, a population which is comparably small and for which published evidence is scarce [13]. While findings from this study may not necessarily be directly applicable to other settings, they point to community level service delivery issues that warrant careful attention when promoting the management of severe childhood illness in African settings.

In conclusion, this research provides context on treatment seeking for children with suspected severe malaria in a northern Nigerian setting, where children visiting a PHC were significantly more likely to die than those attending a CORP. In the context of weak healthcare systems, delay in treatment seeking, higher illness severity in children visiting PHCs, and the inability of PHCs to provide appropriate care, are all likely important drivers of high case fatality. Promoting prompt treatment seeking and strengthening PHCs, referral, and post-referral care are all critical to prevent deaths in children attending community healthcare services.

DATA AVAILABILITY STATEMENT

The datasets generated and/or analysed during the current study are available from the Zenodo repository (<https://doi.org/10.5281/zenodo.5733005>) upon reasonable request to the corresponding author.

ETHICS STATEMENT

The studies involving humans were approved by the Research Ethics Review Committee of the World Health Organization (WHO ERC, No. ERC.0003008), the Health Research Ethics Committee of the Adamawa State Ministry of Health, Nigeria (S/MoH/1131/I), the National Health Research Ethics Committee of Nigeria (NHREC/01/01/2007-05/05/2018), and the Scientific and Ethical Review Committee of the Clinton Health Access Initiative, USA (No. 112, 21 Nov 2017). The studies were

conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin. The study is registered on ClinicalTrials.gov (NCT03568344, 22/06/2018).

AUTHOR CONTRIBUTIONS

CL, CB, MH, AS, and EO conceptualized and designed the study. MH, EO, AS, ML, MK, CB, and CL developed the methodology. EO, KA, CO, OY, and NB led and supervised the data collection. EO, OY, CF, OW, and FC provided project management and coordination support. EE, FC, CF, and OW supported the implementation of the study. MH, AS, NB, KA, CO, OY, GD, EO, and TL curated the data and contributed to data analysis. TL and MK led the data analysis. TL and EO wrote the manuscript. All authors contributed to the article and approved the submitted version.

FUNDING

The author(s) declare that financial support was received for the research and/or publication of this article. This study was funded by Unitaid.

CONFLICT OF INTEREST

Authors EO, KA, OY, and CO were employed by the company Akena Associates.

The remaining authors declare that they do not have any conflicts of interest.

ACKNOWLEDGMENTS

We would like to acknowledge the children and their caregivers who participated in the study and the large number of health workers, data collectors, local coordinators, local CHAI, UNICEF, and WHO colleagues, and colleagues at the Adamawa State Primary Healthcare Development Agency who made this work possible. We would also like to thank Amanda Ross for her statistics support. A pre-print version of this article has been published on medRxiv, 2021, 12.01.21267130 (<https://doi.org/10.1101/2021.12.01.21267130>).

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.ssph-journal.org/articles/10.3389/ijph.2025.1607697/full#supplementary-material>

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