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Co-Infection of Lassa Fever-Malaria (LF) in Endemic Settings: Influence on LF Case Detection in Health Facilities in Ondo State, Nigeria

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Abstract *In malaria-endemic settings, a positive malaria result may explain fever while Lassa fever (LF) remains clinically possible. This study assessed LF-malaria co-infection, probable missed LF suspicion, and diagnostic delays in selected health facilities in Ondo State, Nigeria. A convergent mixed-methods design combined retrospective review of 463 LF and malaria records from 2021 – 2023 across 10 purposively selected facilities in five high-burden LGAs with nine key-informant interviews. Co-infection required positive LF and malaria laboratory results. Quantitative data were analysed using descriptive statistics, chi-square tests and logistic regression; qualitative findings were analysed thematically and integrated through a joint display. All 463 records were purposefully selected as confirmed LF cases. Of these, 297 (64.1%) had positive LF and malaria results. Malaria was suspected in 440 (95.0%) records, and 324 (70.0%) had prior malaria treatment. Probable missed LF suspicion occurred in 103 (22.2%) records. Malaria positivity was associated with missed suspicion (adjusted odds ratio [aOR] 5.30, 95% CI 2.13–13.19; p < 0.001). Interviews highlighted symptom overlap, malaria-first reasoning, treatment failure, restricted RT-PCR access, specimen-transport barriers, notification gaps and uneven refresher training. Overall, 386 (83.4%) patients recovered and 53 (11.4%) died; the case-fatality proportion among confirmed LF records was 11.4%. In this selected sample, malaria appeared to mask LF rather than establish an independent cause of mortality. Malaria confirmation should not close the LF detection pathway. Parallel assessment, timely LF specimen collection, reliable transport, effective surveillance communication and practical diagnostic algorithms may support earlier detection.*

Keywords *Co-Infection, Lassa Fever, Malaria, Mixed-Methods, Suspicion-Index.*

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Research in Context

Evidence Before this Study

Early LF is clinically non-specific and can resemble malaria and other acute febrile illnesses. Malaria-LF co-infection has been documented in Nigeria, but less is known about how malaria positivity affects the first clinical decision to suspect LF within routine care. Previous Nigerian and Ondo State studies have described LF burden, delayed presentation, clinical overlap and healthcare-worker knowledge gaps, but the pathway linking malaria diagnosis to missed LF suspicion has received less attention [1-5].

Added Value of this Study

This study links record-based evidence with accounts from state, LGA and facility-level actors involved in LF detection. The quantitative analysis identified a sizeable association between malaria positivity and probable missed LF suspicion. The interviews then showed how the association can arise in practice: malaria is considered first, a positive result can reduce further suspicion, and LF is often reconsidered only after symptoms persist, treatment fails or the patient returns. The study therefore treats missed detection as a pathway problem rather than as an isolated clinician error.

Implications of All the Available Evidence

In a LF- and malaria-endemic setting, a positive malaria result should not function as a rule-out test for LF. A practical response is a dual-pathway fever algorithm in which malaria testing continues, while LF assessment is triggered by clinical persistence, severity, epidemiological exposure, repeat attendance or other compatible features. Where the trigger is met, LF specimen collection should not wait for several failed malaria treatment courses.

Introduction

Lassa fever is an acute zoonotic viral haemorrhagic disease of public health importance in West Africa. Nigeria experiences recurrent outbreaks and remains one of the countries carrying the greatest reported burden. Ondo State has repeatedly been identified as a high-burden setting, with spatial clustering and recurrent transmission documented in several local government areas [6]. The continuing burden makes early case recognition important for treatment, infection prevention and control, surveillance and outbreak response.

The first clinical encounter with LF is often difficult. Fever, weakness, headache, vomiting, diarrhoea, myalgia and sore throat are common early manifestations. These features overlap with malaria and other acute febrile illnesses [7-10]. Bleeding, shock, facial oedema and organ dysfunction can increase clinical suspicion, but waiting for such features risks losing the period when early recognition is most useful. Delayed presentation and delayed recognition have been associated with poorer clinical trajectories among Nigerian LF patients [2, 4].

Malaria creates a particular diagnostic context. It is common, familiar and routinely testable at many points of care. LF requires a different chain of action: clinical suspicion, notification, safe specimen collection, transport and laboratory confirmation, often through a centralized molecular testing network. A malaria result can therefore be correct without being complete. A patient can have malaria, LF or both. Nigerian evidence has previously documented malaria parasitaemia among LF patients [5, 11, 12].

The clinical challenge is not simply symptom overlap. It also concerns how clinicians respond to uncertainty. Diagnostic reasoning literature describes premature closure as a situation in which an initially plausible explanation receives disproportionate weight before alternative explanations have been adequately considered [13]. In malaria-endemic settings, the high prior probability of malaria can make this tendency understandable. The public health problem arises when a positive malaria result ends the search even though the

patient remains clinically or epidemiologically compatible with LF.

The health-system context can reinforce this process. Donabedian's structure–process–outcome model provides a useful way of viewing the pathway. Laboratory availability, trained personnel, transport and reporting systems form part of the structure. Clinical assessment, testing, notification, sample collection and referral form the process. Missed suspicion, delayed confirmation, repeated treatment and adverse outcomes are possible consequences [14]. Evidence from Ondo State has already documented knowledge gaps and limitations in infection-prevention resources among healthcare workers [1, 15].

This study was designed to examine the interaction more directly. It focused on the occurrence of LF-malaria co-infection, the characteristics of patients and healthcare settings associated with poor detection, the dynamics of missed LF suspicion and healthcare workers' accounts of how cases move through the diagnostic pathway. The central proposition was not that malaria treatment is inappropriate. Rather, it was that malaria-focused clinical reasoning can become a masking mechanism when LF remains possible. The study, therefore, addressed four linked objectives: (i) determine the proportion of LF and malaria co-infection, and probable missed cases of LF in 5 endemic LGAs from 2021 to 2023 in Ondo State; (ii) establish the socio-demographic characteristics and care-seeking behaviour of suspected febrile illness cases associated with case detection of LF in endemic LGAs in Ondo State; (iii) understand the practices of health workers and facility structures or capacities associated with LF case detection among selected health facilities in Ondo State; and (iv) to explore health workers' perspectives on clinical decision-making or suspicion index, case/patient pathways, and clinical and health-system factors contributing to missed or delayed detection of LF in selected health facilities in Ondo State. The study hypothesized that malaria positivity and malaria-first treatment pathways would be associated with a greater probability of missed LF suspicion.

Materials and Methods

Study Design and Setting

A convergent mixed-methods design was used. The quantitative strand retrospectively linked LF surveillance records with outpatient and malaria records. The qualitative strand used key-informant interviews with public-health leaders, disease-surveillance and notification officers and frontline healthcare workers. Both strands examined the same broad phenomenon from different positions in the health system and were integrated during interpretation through a joint display [16, 17].

The study was conducted in Ondo State, south-western Nigeria. Five high-burden LGAs were represented: Owo, Ose, Akure South, Akure North and Akoko South-West. Ten facilities were included across tertiary, secondary, primary and private sectors. The purposive selection was intended to follow the diagnostic pathway across levels of care. It was not designed to produce a population-representative estimate for Ondo State.

Quantitative Population, Sampling and Data Sources

The state line list recorded 161, 375, and 439 confirmed Lassa fever (LF) cases in the selected LGAs in 2021, 2022, and 2023, respectively, totaling 975 cases. Of these, 463 records were verified at the selected facilities and included in the quantitative analytic dataset following purposive selection and linkage with outpatient, malaria, laboratory, and surveillance records. The remaining 512 line-listed cases were not represented in the verified analytic dataset because of the cases were recorded against other health facilities within the selected endemic LGA. Poor quality of data such as incomplete data entry and missing variables that prevented record triangulation were also

among the possible reasons for this discrepancy.

Therefore, the 463 records constituted the verified analytic sample rather than the complete line-listed population of confirmed LF cases. Data were abstracted on sociodemographic characteristics, clinical presentation, diagnostic procedures, malaria treatment, delays, and outcomes. Inconsistent labels and duplicate fields were cleaned during data processing. Two implausible age values were excluded from age-specific summaries but retained in other analyses.

Operational Definitions

Laboratory-confirmed LF was defined as a positive LF laboratory-result field. Primary co-infection required positive LF and positive malaria laboratory results in the same abstracted record. This direct laboratory definition was used because the dedicated co-infection field did not agree perfectly with the two laboratory fields. Probable co-infection without direct laboratory confirmation was not included in the primary estimate.

The study abstraction instrument operationalized LF case-definition fulfilment as fever of at least 38°C that failed to respond to appropriate antimalarial and antibiotic treatment within 48 – 72 hours, particularly during the peak season or in the presence of epidemiological risk, or compatible illness accompanied by recent rodent exposure or contact with a probable or confirmed case. This reflects the study instrument and the principles of national and international suspected-case definitions, recognizing that case guidance evolves [16].

Probable missed LF suspicion was defined as a record indicating that the patient met the study's operational LF case definition but LF was not suspected at initial assessment. The term probable is important because absence of documentation does not prove that the clinician did not consider LF. Delayed suspicion was defined as a documented delay of more than 24 hours before LF suspicion or specimen collection.

Qualitative Participants and Data Collection

Nine identifiable interviews were analyzed. Participants included two state-level public-health leaders, two LGA surveillance officers and five facility-based informants from tertiary, secondary, primary and private care. One intended participant did not have a separately identifiable transcript and was not reconstructed. Interviews explored LF knowledge, differentiation from malaria, missed cases, diagnostic tools, training, notification, surveillance, co-infection, patient outcomes and recommendations.

Participants gave recorded verbal consent and transcripts were de-identified using participant codes. Quotations were edited only lightly to remove repeated words and improve readability while preserving their substantive meaning.

Quantitative and Qualitative Analysis

Categorical variables were summarized using frequencies and percentages. Age was described using the mean, standard deviation, median and range after restriction to plausible values. Pearson chi-square tests examined bivariate associations. A multivariable binary logistic regression model for probable missed LF suspicion included year, facility type, residence, LF diagnostic capacity, malaria-test positivity and previous malaria treatment. Adjusted odds ratios, 95% confidence intervals and two-sided p values were reported. Because the facility and LGA strata were purposively selected and some cells were sparse, estimates were interpreted as sample-specific associations rather than population trends.

Qualitative data were analyzed using reflexive thematic analysis [18]. Coding focused on recurring clinical and health-system patterns, contradictions and differences across stakeholder levels. Theme counts represent the

number of nine transcripts containing substantive evidence for each theme. They are presented for analytic transparency and not as statistical prevalence.

Integration occurred after separate analyses. Quantitative associations were compared with qualitative explanations to identify convergence, complementarity and divergence. The purpose was to determine not only whether a statistical pattern was present but also how it could arise in routine practice.

Ethics and Reporting

The retrospective records were de-identified. Interview participation was voluntary and based on recorded consent. The final journal version should insert the exact approving ethics committee, approval number and approval date from the approved study documents. The quantitative reporting was prepared with reference to STROBE and the qualitative reporting with reference to COREQ [19, 20].

Results

Characteristics of the Analytic Sample

In Table 1 below, the analytic dataset contained 463 records. The mean age was 37.8 years (SD 20.2), the median was 35 years and the observed range was 0–91 years among records with plausible ages. Females accounted for 239 (51.6%) records and males for 224 (48.4%). Owo contributed 327 (70.6%) records. This concentration reflects the purposive inclusion of high-burden facilities and should not be interpreted as the population distribution of LF in the state.

Table 1. Selected Characteristics of the Retrospective Analytic Sample (N = 463, Mean Age = 37.8 years, Median Age = 35 years and Observed Range = 0–91 years)

Characteristic	n	%
Female	239	51.6
Male	224	48.4
Age <15 years	53	11.5
Age 15–24 years	78	16.9
Age 25–44 years	161	34.9
Age ≥45 years	169	36.7
Tertiary facility	339	73.2
Secondary facility	25	5.4
Primary health-care facility	51	11.0
Private facility	48	10.4
Urban residence	397	85.7
Rural residence	66	14.3
Year 2021	116	25.1
Year 2022	149	32.2
Year 2023	198	42.8

Clinical Presentation and the Initial Diagnostic Pathway

The Table 2 below shows fever was recorded in 453 (97.8%) records. Headache occurred in 214 (46.2%), weakness in 134 (28.9%) and body pain in 112 (24.2%). Bleeding was recorded in only 15 (3.2%) records. The clinical picture was therefore dominated by non-specific symptoms rather than by a classic haemorrhagic presentation.

Malaria was suspected in 440 (95.0%) records and a malaria test was documented in

438 (94.6%). Rapid diagnostic testing accounted for 365 (78.8%) recorded malaria tests and microscopy for 63 (13.6%). Malaria treatment was recorded in 302 (65.2%) records. LF was suspected at first contact in 262 (56.6%) records and was not suspected in 201 (43.4%).

Table 2. Clinical Presentation, Diagnostic Pathway and Missed-Detection Indicators (N = 463)

Indicator	n	%
Symptom		
Fever	453	97.8
Headache	214	46.2
Weakness	134	28.9
Body pain	112	24.2
Vomiting	84	18.1
Diarrhoea	62	13.4
Joint pain	41	8.9
Bleeding	15	3.2
Diagnostic pathway		
Malaria suspected	440	95.0
Malaria test documented	438	94.6
Malaria result positive	304	65.7
Malaria treatment given	302	65.2
LF suspected at first contact	262	56.6
LF test requested	461	99.6
Missed/delayed detection		
Probable missed LF suspicion	103	22.2
Documented delay >24 hours	33	7.1
Previous malaria treatment before LF confirmation	324	70.0
Symptoms persisted after malaria treatment	359	77.5

Laboratory Confirmation, Co-Infection and Probable Missed Suspicion

All the purposively selected 463 records were confirmed positive with LF laboratory result. Direct cross-classification of the LF and malaria laboratory fields identified 297 patients positive for both infections. These 297 records represented 64.1% of the 463 laboratory-confirmed LF records. The dedicated co-infection variable classified 311 (67.2%) records as confirmed co-infection, but the direct laboratory definition was retained for the main analysis because it was biologically more explicit.

A total of 103 records (22.2%) met the probable missed-suspicion definition. From the analysis, 103 records were drawn from the confirmed LF sample and 77 (74.8%) were malaria-positive. Five were LF-negative, one had testing not done and one had no recorded LF result. The finding indicates that the missed-

suspicion measure frequently preceded later LF confirmation.

The recorded proportion of probable missed suspicion of LF was 5.2% in 2021, 14.8% in 2022 and 37.9% in 2023 – an increasing trend that is quite worrisome (Figure 1). Because facility composition and abstraction coverage varied by year, these values should rather not be interpreted as a statewide temporal trend. They show instead that probable missed-suspicion records were concentrated in the later part of the selected analytic sample.

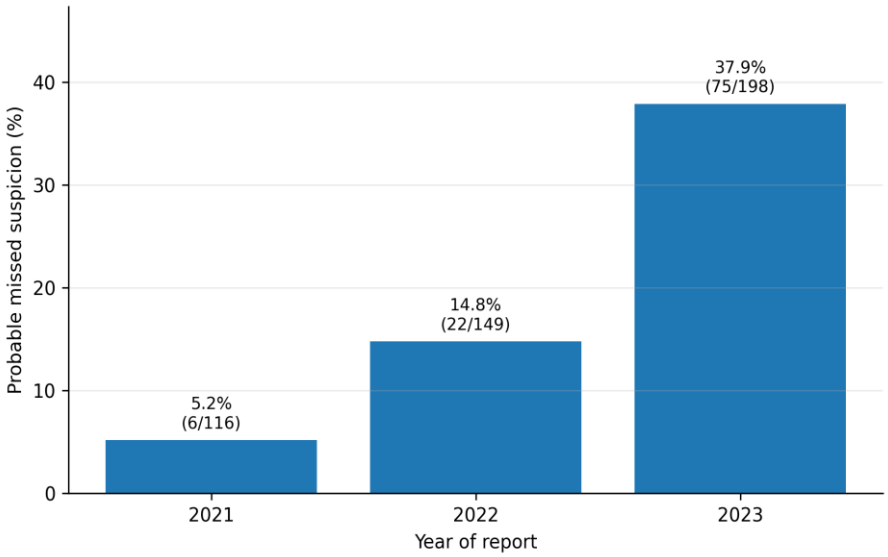

Figure 1. Probable Missed Lassa Fever Suspicion by Year of Report

Percentages use all linked records within each year. Facility composition and abstraction coverage varied over time.

(Originally created by me – Saiki Adinoyi Musa)

Factors Associated with Probable Missed LF Suspicion

At bivariate level shown in Table 3, probable missed suspicion was associated with LGA, facility type, first point of care, residence, occupation, year, recorded LF diagnostic capacity, malaria positivity and previous malaria treatment. Age group, sex and education did not meet the 5% significance threshold. The stronger pattern across service and diagnostic variables than across basic demographic variables points towards a health-system and case detection-pathway explanation.

Table 3. Bivariate Associations with Probable Missed LF Suspicion

Factor	χ^2	df	p-value
Age group	0.626	3	0.891
Sex	0.005	1	0.941
Local government area	41.903	4	<0.001
Facility type	56.434	3	<0.001
First point of care	12.788	4	0.012
Residence	4.748	1	0.029
Education	7.172	3	0.067
Occupation	12.798	5	0.025
Year of report	52.344	2	<0.001
LF diagnostic capacity	11.611	1	<0.001

Malaria-test positivity	4.358	1	0.037
Previous malaria treatment	4.216	1	0.040

In the adjusted model shown in Table 4, malaria-test positivity remained associated with probable missed LF suspicion (aOR 5.30, 95% CI 2.13 – 13.19; $p < 0.001$). Compared with 2021, the odds were higher in 2022 and 2023. Primary health-care records had lower adjusted odds than tertiary-facility records in the selected sample. Private-facility estimates approached the conventional threshold but did not reach statistical significance. Previous malaria treatment was not independently associated with missed suspicion after adjustment. The large year effects and wide confidence intervals in some strata indicate sparse-cell instability and should not be interpreted as evidence of a secular statewide increase.

Table 4. Multivariable Logistic Regression for Probable Missed LF Suspicion

Predictor	**Comparison**	**aOR**	**95% CI**	**P**
Year	2022 vs 2021	4.07	1.55–10.68	0.004
	2023 vs 2021	29.39	10.93–79.06	<0.001
Facility	Secondary vs tertiary	1.19	0.43–3.28	0.739
	PHC vs tertiary	0.07	0.01–0.52	0.010
	Private vs tertiary	2.43	0.99–5.96	0.052
Residence	Urban vs rural	0.68	0.33–1.40	0.293
LF capacity	No vs yes	2.07	0.67–6.42	0.208
Malaria test	Positive vs non-positive	5.30	2.13–13.19	<0.001
Previous malaria treatment	Yes vs no	1.02	0.42–2.45	0.968

Patient Outcomes

Overall, 386 (83.4%) patients recovered, 53 (11.4%) died, 20 (4.3%) were referred and four (0.9%) had unknown outcomes. Among the 463 laboratory-confirmed LF records, 53 deaths yielded an observed case-fatality proportion of 11.4%. This is a sample-specific case-fatality proportion and not a population case-fatality rate because the analytic sample was purposively assembled.

In an exploratory unadjusted comparison restricted to laboratory-confirmed LF records, death occurred in 46 of 297 co-infected records (15.5%) and six of 106 records without a positive malaria result (5.7%). The crude odds ratio was 3.05 (95% CI 1.26–7.38; Fisher exact $p = 0.011$). This comparison is hypothesis-generating. The dataset did not adequately adjust for diagnostic delay, referral severity, comorbidity, viral load, dehydration, treatment timing or facility selection. The result therefore does not establish that malaria independently caused excess mortality.

Qualitative Findings

As shown in Table 5, nine interviews were analysed. Participants occupied different positions in the detection system, but their accounts converged on a common problem: early LF often looks ordinary, while malaria is familiar and easy to test. The resulting pathway was not described as the consequence of a single clinician error. Participants linked missed detection to symptom ambiguity, malaria-first routines, access to testing, specimen transport, surveillance relationships, patient movement between providers and uneven training.

Table 5. Themes Derived from Key-Informant Interviews

Theme	Participants	Analytic Meaning
Symptom overlap and early diagnostic ambiguity	9/9	Early LF resembled malaria through fever, headache, weakness, vomiting, diarrhoea and body pain. Bleeding or facial swelling was often described as a later signal.
Malaria-first diagnostic pathway and masking	9/9	Malaria was commonly considered first. A positive result could reduce suspicion for LF and redirect attention to antimalarial treatment.
Delayed suspicion after treatment failure or repeat visits	8/9	LF was often reconsidered after 24–72 hours of non-response, repeated treatment, discharge and return or another point-of-care encounter.
Restricted RT-PCR access, specimen transport and turnaround	9/9	Malaria RDTs were more accessible, whereas LF confirmation depended on centralized molecular testing, transport, cold chain, cost and turnaround.
Knowledge, experience and refresher-training gaps	9/9	Training existed but coverage was uneven. Staff movement and limited co-infection-specific content created a continuing need for practical retraining.
Surveillance notification and communication gaps	7/9	Late clinician notification, weak facility–DSNO links, workload and limited reporting tools delayed surveillance action.
Patient-level barriers and delayed care seeking	7/9	Self-treatment, patent medicine vendors, traditional remedies, stigma, distance and transport costs lengthened the pre-diagnostic journey.
Co-infection affected detection more consistently than prognosis	8/9	Participants agreed that co-infection could obscure or delay diagnosis but differed on whether malaria independently worsened outcomes once both infections were treated.
Priority interventions	9/9	Participants prioritized recurrent training, visible algorithms, active case search, specimen transport, decentralized testing, clinician–surveillance networks and community education.

Excerpts from Frontline and Surveillance Narratives

"There are several instances where you think it is malaria initially. You treat the patient for malaria. Sometimes we even discharge the patient. But then the patient returns, not getting better; instead, the patient is getting worse."

PID-01-001, state public-health leader

The excerpt captures the central trajectory identified in the interviews. LF suspicion often developed after the malaria pathway had already begun. The problem was not necessarily the initial decision to test or treat malaria. The missed opportunity arose when persistent illness did not trigger an earlier parallel consideration of LF.

"At presentation, we did a malaria test and it was positive, so every attention was focused on malaria. It was when the patient had received antimalarial and other

medication for two days without response that we thought about Lassa fever.

PID-04-007, secondary-facility focal clinician

This account illustrates how a positive malaria result can become a stopping point in clinical reasoning. It also explains why treatment failure emerged repeatedly in the qualitative data as a practical trigger for LF suspicion.

"Some may feel that since this person is positive for malaria, there is no need to suspect Lassa. On a good day, it should not be so."

PID-02-004, local-government surveillance officer

The statement is particularly important for interpreting the quantitative association between malaria positivity and probable missed suspicion. It points to a change in the meaning attached to the malaria result rather than to a problem with malaria testing itself.

"That timely response is still bound to the transportation of the sample. If you remove that impediment, every other thing can move. That is a major problem."

PID-04-007, secondary-facility focal clinician

Once LF suspicion was raised, the next delay could occur outside the consulting room. Sample transport, packaging, refrigeration, weekend schedules, consumables and communication with surveillance teams were repeatedly described as practical constraints.

Discussion

Principal Findings

The central finding of this study is that the relationship between malaria and LF in the selected Ondo State facilities is not limited to biological co-occurrence. It also operates through the diagnostic pathway. Among 463 laboratory-confirmed LF records, 297 had positive malaria and LF laboratory results in the same record. This 64.1% proportion is higher than the 37% reported in an earlier Nigerian conference series [5]. The difference should not be interpreted as evidence of a statewide increase. The present estimate comes from a purposively selected linked-record sample, a different period and a direct laboratory definition of co-infection.

The study's more important contribution is the link between co-infection and detection. Probable missed LF suspicion occurred in 103 of 463 records (22.2%), and 96 of those records were later LF laboratory-positive. Malaria positivity remained associated with missed suspicion after adjustment, with approximately fivefold higher odds. The qualitative strand gave this statistical finding a clinical sequence: fever was interpreted as malaria, malaria was tested or treated, the positive result could reinforce the initial explanation, and LF was reconsidered when the expected response did not occur.

This interpretation is consistent with evidence that early LF is difficult to distinguish from other febrile illnesses [7, 8]. It also fits the concept of premature diagnostic closure described by Croskerry [13]. The present study adds a setting-specific explanation. In a malaria-endemic environment, diagnostic closure does not necessarily arise because clinicians lack knowledge of LF. It can arise because the common diagnosis is plausible, rapidly testable and reinforced by the clinical routine.

The study also found that 70.0% of records had previous malaria treatment before LF confirmation and 77.5% documented persistence of symptoms after malaria treatment. The qualitative accounts were closely aligned with these figures. Eight of nine participants described reconsideration after non-response, repeated attendance or deterioration. Treatment failure therefore appears to function as a practical trigger for LF suspicion. The concern is that waiting for that trigger consumes time.

Co-Infection as a Diagnostic-Masking Mechanism

The high co-infection proportion within the selected analytic sample supports the need to treat malaria and LF as potentially concurrent diagnoses in endemic facilities. Earlier Nigerian evidence identified malaria parasitemia among confirmed LF cases [5, 21]. Studies in Ondo State have also reported LF–malaria co-infection and clinical severity concerns [5]. The present study extends this evidence by showing that co-infection can matter before treatment outcomes are considered. It can affect the route through which LF is recognized.

Rugarabamu et al. (2022) reported the difficulty of distinguishing malaria from viral haemorrhagic fevers when clinical presentations overlap. The qualitative evidence in the present study provides a similar account from routine care. Participants repeatedly described fever, headache, weakness, vomiting and body pain as features that could support a malaria diagnosis without excluding LF. The absence of bleeding at early presentation is also relevant. Only 3.2% of records documented bleeding, suggesting that reliance on haemorrhagic features alone would miss much of the clinically difficult presentation.

The implication is not to replace malaria-first probability with indiscriminate LF testing. Such an approach would be inefficient and difficult to sustain. The more defensible response is to prevent malaria confirmation from becoming a diagnostic stopping rule. The clinical question should change from “Is this malaria?” to “Does malaria fully explain this illness, given the clinical course and epidemiological context?”

Malaria Positivity and Missed LF Suspicion

Malaria-test positivity was the strongest independent diagnostic-pathway association in the adjusted model. Patients with positive malaria results had higher odds of probable missed LF suspicion. This finding is consistent with the qualitative theme of malaria-first reasoning, which was present in all nine interviews. Participants described situations in which the positive malaria result appeared to settle the diagnosis until the patient failed to improve.

The result should be interpreted carefully. A positive malaria test is not itself a diagnostic error. The study does not show that malaria testing should be reduced or that antimalarial treatment caused LF to be missed. Instead, the result suggests that malaria positivity changes the clinical context in which LF is considered. The distinction matters because the practical intervention is not to remove malaria from the pathway. It is to keep the LF pathway open when risk persists.

The finding is also compatible with earlier observations that malaria and LF share overlapping clinical features and that diagnostic schemes for viral haemorrhagic fevers must account for common febrile illnesses [22]. In this study, the strongest quantitative signal came from malaria positivity, while the qualitative accounts explained the cognitive and operational process behind it.

Rural Residence, Access and the Accumulation of Delay

Rural residence was associated with delayed LF suspicion in the thesis analysis. Although it did not remain an independent predictor of probable missed suspicion in the reconciled adjusted manuscript model, the direction of the evidence remains relevant. The qualitative data identified structural barriers that help explain why location can prolong the diagnostic pathway.

Participants described centralized PCR testing, specimen-transport costs, transport delays, cold-chain requirements, shortages of consumables and difficulty accessing testing centres. These barriers are consistent with the wider Nigerian literature on delayed LF recognition and presentation [2-4, 23]. The issue is therefore not simply whether a clinician

knows LF. A knowledgeable clinician still faces delay if the facility lacks a functioning route from suspicion to sample collection, transport and result.

The findings also fit Donabedian's structure–process–outcome perspective. Diagnostic capacity, trained personnel and transport arrangements are structural conditions. Clinical reassessment, notification and specimen referral are processes. Missed suspicion and delayed confirmation are outcomes of that system. Improving one component without the others is unlikely to remove the entire delay.

Healthcare-Worker Knowledge, Experience and Clinical Reasoning

The interviews showed that healthcare workers generally recognized LF but did not always apply suspicion early in the case detection pathway. Training existed, yet participants described uneven coverage, staff turnover and a continuing need for practical refresher training. This is consistent with previous evidence of knowledge gaps among healthcare workers in Ondo State [1, 15, 24].

The findings suggest that training should move beyond factual awareness. Healthcare workers need to practice decisions that are likely to occur in real consultations. They need to recognize when malaria and LF should be considered together, how to interpret a positive malaria result without closing the differential, when persistent fever should trigger reassessment and how to activate sample collection and notification.

This is why a visible case-detection algorithm is important. Knowledge that remains in training materials but is not available at the point of care is less likely to influence a time-pressured decision. The qualitative participants themselves prioritized visible algorithms, recurrent training, active case search and stronger clinician–surveillance links.

Treatment Pathways and Repeated Healthcare Visits

Previous malaria treatment was common before LF confirmation, and most records documented persistence of symptoms after treatment. In the thesis analysis, some treatment variables, including ACT and adjunct care, showed associations with missed LF cases. The adjusted manuscript model did not retain previous malaria treatment as an independent predictor. This apparent difference is important. It suggests that treatment variables are better interpreted as markers of the clinical decision pathway than as pharmacological causes of missed LF detection.

The qualitative accounts support this interpretation. Participants described escalation from oral antimalarials to injectable therapy and repeated treatment before LF was considered. The practical problem is the time consumed while the diagnosis remains anchored on malaria. When the patient returns after treatment failure, the opportunity for earlier LF suspicion has already been lost.

This pattern also explains why repeated healthcare visits matter. The patient may move between public and private facilities, patent medicine vendors and other providers before reaching a facility with LF diagnostic capacity. One private-facility informant captured the patient-side component: "One thing that prevents early diagnosis is the patient factor. They keep treating the so-called malaria and typhoid illness before they come." The diagnostic pathway therefore begins before the patient reaches the LF-capable facility.

Patient Outcomes and the Limits of Causal Interpretation

The observed case-fatality proportion among laboratory-confirmed LF records was 11.4%. Death was more frequent among co-infected records in the unadjusted comparison. This finding is compatible with earlier reports that LF severity and outcomes are influenced by timing of presentation and clinical care [2, 4].

However, the present study cannot establish that malaria independently caused mortality.

The outcome comparison did not adequately control for diagnostic delay, viral load, organ dysfunction, comorbidity, dehydration, referral severity or treatment timing. The qualitative participants also differed in their views about whether malaria independently worsened prognosis after both infections were recognized and treated. The more defensible interpretation is therefore that co-infection affected detection more consistently than it demonstrated an independent causal effect on mortality.

A prospective cohort would be needed to test whether malaria mediates outcome through delayed LF recognition. Such a study should measure malaria parasite burden, LF viral load, clinical severity, time from symptom onset to presentation, time to LF suspicion, time to specimen collection, time to treatment and subsequent outcomes.

Mixed-Methods Integration

The two strands converged around a diagnostic-masking mechanism. Quantitatively, 22.2% of records met the probable missed-suspicion definition, 70.0% had previous malaria treatment and malaria positivity was associated with more than fivefold higher adjusted odds of missed suspicion. Qualitatively, participants reconstructed the sequence behind those numbers. Malaria was considered first. A positive result could appear reassuring. LF was reconsidered after non-response, repeat attendance or deterioration.

The health-system findings also converged. Facility type, LGA, first point of care and recorded diagnostic capacity showed quantitative associations at the bivariate level, while interviews described centralized RT-PCR, transport costs, cold-chain requirements, staff turnover, notification delays and uneven reporting tools. There was a meaningful divergence on outcomes. The quantitative data showed a crude association between co-infection and death, but the interviews did not establish that malaria independently worsened prognosis after both conditions were treated (See Table 6).

Table 6. Joint Display Integrating Quantitative and Qualitative Findings

Domain	Quantitative Evidence	Qualitative Explanation	Integrated Implication
Malaria positivity and missed suspicion	aOR 5.30 (95% CI 2.13–13.19)	Positive malaria results could reduce consideration of LF.	Treat malaria, but retain an LF trigger when risk persists.
Treatment failure and repeat attendance	70.0% had previous malaria treatment; 77.5% had persistent symptoms.	LF was often reconsidered after 24–72 hours, repeat visits or deterioration.	Reassess early and collect LF specimens when indicated rather than waiting for repeated failure.
Diagnostic infrastructure	Missed suspicion varied by facility, first point of care, LGA and diagnostic capacity.	Centralized RT-PCR, transport, cold chain, cost and turnaround were recurring barriers.	Strengthen transport, consumables, turnaround and decentralized capacity where feasible.
Surveillance and workforce	Facility and geographic patterns were stronger than age/sex effects.	Staff turnover, uneven refresher training and weak clinician–DSNO links recurred.	Link training to named surveillance contacts, feedback and active case search.

Outcome	Observed LF case-fatality proportion 11.4%; crude mortality higher with co-infection.	Participants agreed on diagnostic delay but not an independent prognostic effect of malaria.	Treat mortality comparison as exploratory; test causality prospectively.

Proposed Integrated LF–Malaria Case Detection Algorithm for Endemic Settings

The study findings support a facility-level algorithm designed around the main point at which diagnostic masking occurred in the current case detection pathway as shown in Figure 2. The proposed algorithm, shown in Figure 3, does not ask healthcare workers to abandon malaria testing. It introduces a parallel LF pathway whenever the clinical or epidemiological picture remains compatible with LF.

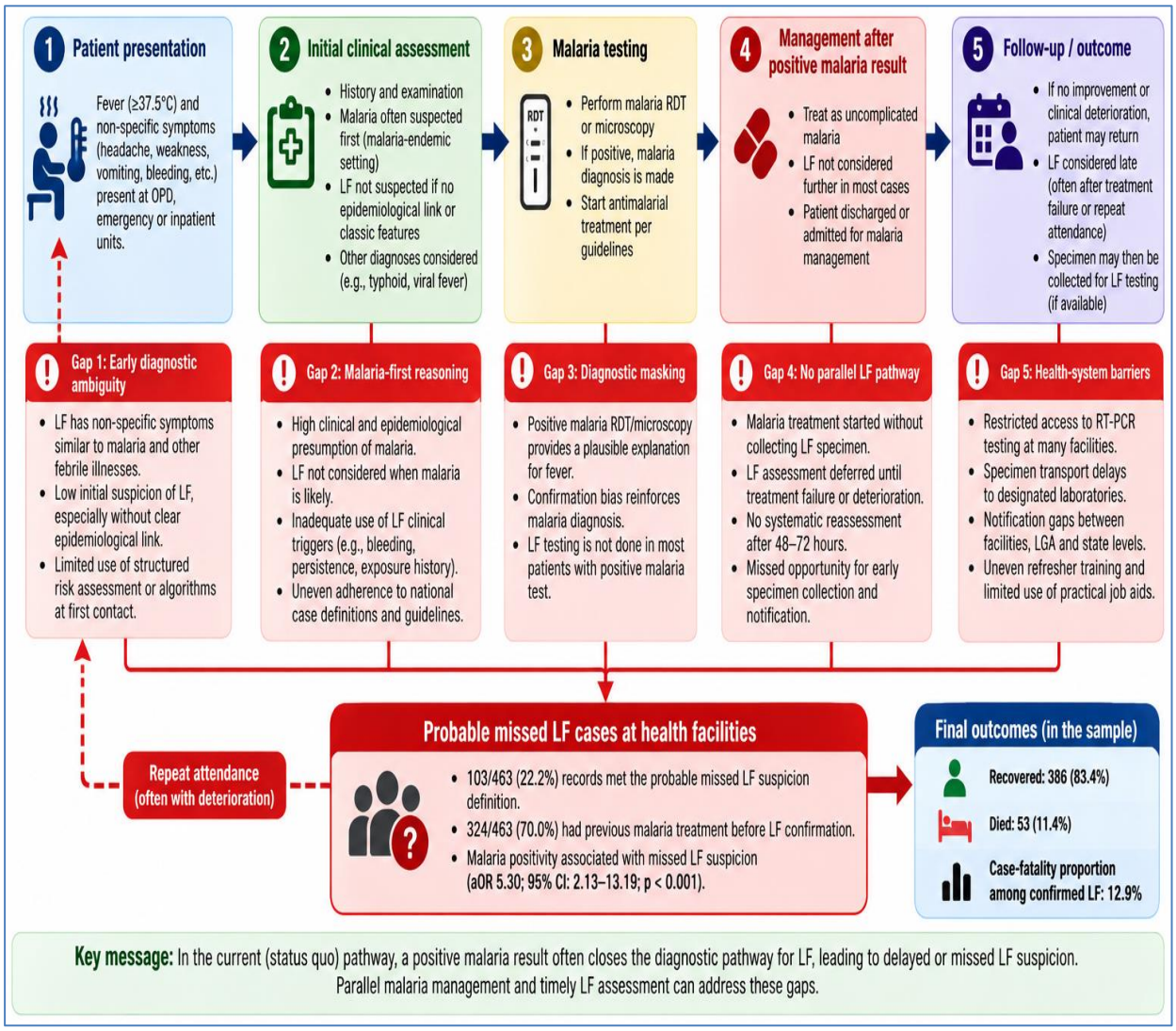

Figure 2. Current Status of Lassa Fever Case Detection Pathway in Endemic Health Facilities Showing Key Gaps that Allows Probable Missed LF Cases

(Originally created by me – Saiki Adinoyi Musa)

https://doi.org/10.21522/TIJAR.2014.13.04.Art024

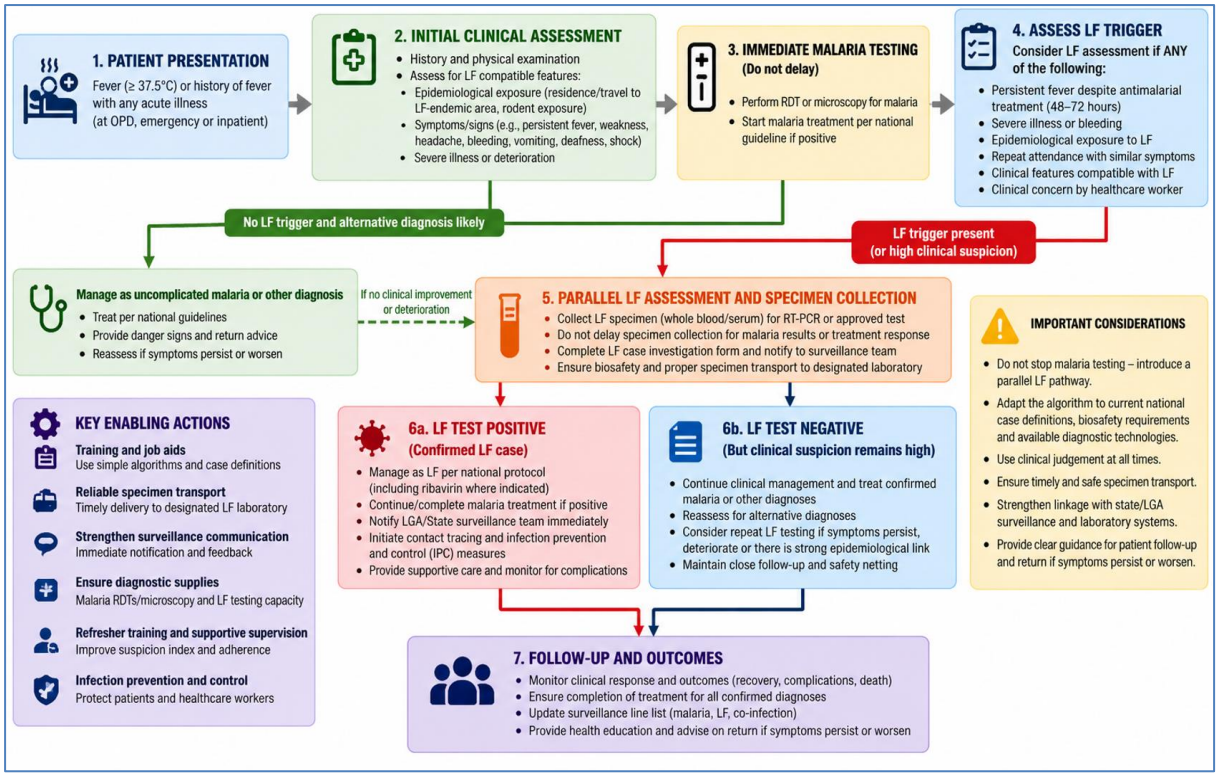

Figure 3. Proposed Integrated LF–Malaria Case-Detection Algorithm for Endemic Health Facilities

(Originally created by me – Saiki Adinoyi Musa)

Implications for Clinical Practice and Surveillance

The proposed pathway responds directly to the study's most consistent finding: malaria confirmation should not automatically close the LF diagnostic process. In practice, this means that a patient with a positive malaria result and persistent fever should not necessarily receive another course of malaria treatment without reassessment. The clinician should ask whether the clinical course remains compatible with LF and, where the trigger is met, collect the LF specimen promptly.

Implementation requires more than placing an algorithm on a wall. Facilities need appropriate sample-collection materials, clear notification channels, reliable specimen transport, feedback from laboratories and continuous training. State and LGA surveillance teams should also use active case search as a learning mechanism. Reviewing missed trajectories with facility teams can show where suspicion, notification or sample collection was lost.

Private hospitals and other first-contact providers should be included in the pathway. The qualitative data showed that patients may move through multiple providers before LF is suspected. A diagnostic strategy that operates only inside public LF treatment centres will therefore miss part of the patient journey. Referral and notification links should extend to private facilities and, where appropriate, community-level referral actors.

Strengths and Limitations

The study has several strengths. It linked LF surveillance, outpatient, malaria and laboratory records across different levels of care. It used a conservative direct laboratory definition of co-infection. It distinguished probable missed suspicion from confirmed LF. It also included state, LGA and facility-level participants, allowing the qualitative strand to explain the operational setting behind the statistical findings. The joint display made convergence

and divergence explicit rather than treating qualitative evidence as a supplementary narrative.

Several limitations warrant caution in interpreting these findings. The retrospective design depended on the completeness and accuracy of registers and case notes. Purposive selection of confirmed LF records with linked malaria information introduced selection bias, limiting representativeness and preventing the observed 64.1% co-infection proportion from being interpreted as statewide prevalence. This selection may also have biased the adjusted association between malaria positivity and probable missed LF suspicion (aOR 5.30). Because the direction and magnitude of this bias cannot be established from the available data, the estimate should be interpreted as an association within the selected analytic sample rather than a population-level effect. The dataset also contained inconsistent labels, duplicate export fields, two implausible age values and some missing laboratory information. The dedicated co-infection field did not fully agree with direct laboratory cross-classification.

The probable missed-suspicion outcome relied on documented fulfilment of the study's case definition and recorded clinical suspicion; undocumented clinical reasoning may therefore have led to misclassification. Uneven facility and LGA representation produced sparse cells and potentially unstable estimates in some regression categories. One intended qualitative participant lacked a separately identifiable transcript, while recall and social-desirability bias may have influenced interview accounts. Finally, the observational design cannot establish that malaria positivity caused missed LF suspicion or mortality. These limitations should be considered when interpreting the findings and assessing their transferability to other facilities and populations.

Conclusion

This study shows that LF–malaria co-infection is common within the selected linked records from high-burden facilities in Ondo State and that the significance of co-infection extends beyond biological overlap. Malaria can influence the way LF is recognized. The clearest signal was the association between malaria positivity and probable missed LF suspicion. The qualitative findings explain how this can happen in practice. Fever is often approached as malaria, a positive result can reinforce that decision and LF is reconsidered when the patient fails to improve, deteriorates or returns.

The findings also show that detection does not depend on clinical reasoning alone. Rural access, diagnostic infrastructure, specimen transport, surveillance communication and healthcare-worker training shape what happens after the patient enters the health system. The study therefore points to a practical change in approach. Malaria should continue to be tested and treated, but a positive malaria result should not close the LF pathway when clinical or epidemiological risk remains. Earlier parallel assessment, prompt LF specimen collection, reliable specimen movement and continuous clinical learning offer a realistic route to reducing missed opportunities.

Recommendations

State Ministry of Health

The Ondo State Ministry of Health should adopt and pilot the proposed integrated LF-malaria case-detection algorithm in high-burden facilities. The algorithm should be incorporated into routine fever assessment rather than reserved for declared outbreaks. The State Epidemiologist and State DSNO should coordinate its implementation with clinical leadership, laboratory services and LGA surveillance teams.

The state should establish a dependable LF specimen-transport system with defined

collection schedules, weekend coverage where needed, appropriate cold-chain arrangements, tracking and clear turnaround targets. Diagnostic strengthening should also include adequate consumables and progressive expansion of molecular testing or validated near-patient options where feasible and safe.

The Ministry should institute recurrent, case-based training for healthcare workers. Training should use real diagnostic trajectories and focus on symptom overlap, co-infection, interpretation of malaria-positive results, treatment failure as a reassessment signal, specimen collection and notification. Training should be linked to named facility surveillance focal persons so that knowledge is connected to action.

The state should strengthen routine monitoring of the diagnostic pathway itself. Surveillance should track not only confirmed LF cases but also time from first presentation to suspicion, notification, specimen collection and confirmation. These indicators would allow the system to identify where delay is accumulating.

Local Government Area level

LGA DSNOs and their assistants should provide supportive supervision to public and private facilities, with particular attention to facilities that serve as first points of contact. Supervisory visits should review whether LF triggers are recognized, whether suspected cases are notified promptly and whether specimens move through the referral system without avoidable delay.

LGA surveillance teams should maintain active case search and use missed trajectories as learning material. When a confirmed LF case is identified, the team should review where the patient first presented, whether malaria was considered, when LF entered the differential, when the specimen was collected and whether notification was timely. The purpose should be improvement rather than blame.

Community and provider communication should also be strengthened. Patients who repeatedly receive treatment for malaria without improvement should be encouraged to return promptly or seek referral. Private clinics and patent medicine vendors should be linked to referral and notification messages because the qualitative findings show that patients often move through these points before reaching LF-capable facilities.

Health-Facility Level

The health facility is the primary intervention point arising from this study. LF focal doctors or nurses, case managers, facility surveillance focal persons, medical officers in private hospitals and Officers-in-Charge of PHCs should use the integrated algorithm as part of routine fever assessment. A malaria-positive result should not automatically terminate LF assessment where fever persists, illness is severe or unusual, epidemiological risk is present, the patient returns after treatment or clinical improvement does not occur within the defined reassessment period.

Where the LF trigger is met, the facility should collect the LF specimen promptly while continuing appropriate malaria care. Notification should occur at the same time. The facility surveillance focal person should maintain a direct communication line with the LGA DSNO and ensure that specimen movement and laboratory feedback are documented.

Facility leaders should incorporate short LF-malaria case reviews into routine clinical meetings. These reviews should examine missed opportunities without assigning individual blame. They should ask simple operational questions: Was LF considered early? Did the malaria result close the differential? Was the LF specimen collected promptly? Was notification made? Did the sample move? Was the result returned to the clinician?

Private facilities should receive the same algorithm, training and referral support as public facilities. This is essential because a

patient can enter the diagnostic pathway outside the public health system and return later with more advanced disease. The study's qualitative findings make this patient movement an important part of the intervention rather than a peripheral issue.

Ethics Approval and Consent to Participate

This work was approved by the Ondo State Health Research Ethics Committee (OSHREC), with assigned number NHREC/Ondo SMH-HREC/02/01/2025 and protocol number OSHREC/18/05/2026/13/05. The retrospective records were de-identified and interview participants provided recorded consent.

Consent for Publication

No personally identifiable information (PII) of any case is reported. Participant quotations are presented using study codes.

Data Availability

The de-identified analytic dataset and coding framework will be made available only in accordance with Ondo State Ministry of Health, participating-facility and applicable data-governance requirements.

Conflict of Interests

All authors declares no conflict of interest.

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Author Contributions

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- Writing of first draft: Saiki Adinoyi Musa
- Manuscript Review: All authors

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