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Improving adherence to severe malaria treatment guidelines in children at a Ugandan regional hospital: assessment of a quality improvement initiative

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Abstract

Background Malaria is the leading cause of hospitalizations and death in Uganda, particularly in children under the age of five. Studies have shown that adherence to the World Health Organization (WHO) guidelines for the management of severe malaria reduces mortality in hospitalized children. This study aimed to determine the impact of targeted interventions on adherence to the WHO severe malaria treatment guidelines in children at a Ugandan hospital as part of a quality improvement initiative.

Methods Interventions included workflow changes, such as obtaining patient blood samples for diagnostic testing by the admitting healthcare provider as well as utilizing patient caregivers to assist nursing staff in timing medications. An additional intervention was the use of an admission checklist sticker. The post-intervention sample was compared to the baseline assessment. The primary outcome was the proportion of patients receiving care consistent with all aspects of the WHO guidelines. Secondary outcomes included the proportion of patients receiving malaria diagnostic testing, those receiving at least 3 doses of artesunate, the timely administration of artesunate, and adherence to other guideline components. Statistical analyses were conducted using GraphPad PRISM 9.0. Comparisons between groups were analysed using Chi-square or Fisher's exact test for categorical variables and Mann-Whitney test for continuous variables.

Results The post-intervention group included 230 patients with a median age of 5 years [4–8], and 58% of patients were male. Adherence to all aspects of the WHO guidelines was achieved in 10% of patients in the post-intervention group compared to 3% of patients in the baseline ($P=0.007$). Appropriate malaria diagnostic testing was performed in 85% of patients post-intervention compared to 66% of patients in the baseline ($P<0.0001$). Patients in the post-intervention group were more likely to receive the minimum 3 doses of artesunate (86%) than in the baseline (74%) ($P=0.008$). Patients in the post-intervention group were more likely to receive artesunate doses on time than in the baseline (dose 2 $P=0.02$, dose 3 $P=0.003$).

Conclusions Targeted, low-cost interventions led to improvement in adherence to severe malaria treatment guidelines. The most notable changes were in malaria diagnostic testing and antimalarial administration.

Keywords Malaria, Severe malaria, Guidelines, Case management, Adherence, Uganda

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Background

Malaria is one of the greatest burdens on the health of children worldwide, and particularly in Uganda. According to the 2023 World Malaria Report of the World Health Organization (WHO), there were 249 million cases of malaria in 2022 in 85 malaria-endemic countries. These cases led to 608,000 deaths, 77% of which were in children under 5 years of age. Uganda accounted for 5% of all malaria cases, making it the 3rd most burdened country after Nigeria and the Democratic Republic of the Congo [1]. In Uganda, among all age groups malaria is the most common cause of outpatient health visits (29.1%), hospital admissions (39.5%), and the most common cause of death in health facilities (10.9%) [2]. In addition, malaria is the leading cause of death in children under the age of 5 in Uganda, with 16.4% of deaths in this age group in health facilities being attributable to the disease [2]. Uganda also seems to be experiencing a shift in the age group most burdened by malaria, with an increase in severe cases in children above 5 years of age in recent years [3].

The WHO has issued guidelines for the identification and treatment of malaria to address this great need [4, 5]. These guidelines are mirrored by the Ugandan national guidelines issued by the Ministry of Health [6]. Evidence to date suggests that adherence to these guidelines in sub-Saharan Africa is generally poor, around 50% at best [7–9]. More encouragingly, a recent study from Sierra Leone demonstrated the ability to improve adherence to a standardized malaria treatment protocol in a resource limited setting with subsequent reduced mortality in hospitalized children with severe malaria. This was achieved by developing targeted interventions based on areas identified as in need of improvement [10]. Indeed, other studies have also demonstrated that improving adherence to WHO guidelines in hospitalized paediatric patients is possible and improves outcomes [11–13]. At Mbale Regional Referral Hospital, a previously-published baseline assessment demonstrated that adherence to guidelines for severe malaria in children was poor at 3% overall [14]. Based on the identified areas of concern in the baseline assessment, targeted interventions have been implemented with particular focus on malaria diagnostic testing and anti-malarial administration. The aim of this study is to assess the impact of these interventions on the adherence to treatment guidelines at the end of the first intervention cycle of this quality improvement initiative.

Methods

This is a retrospective study of children with severe malaria based on a convenience sample of children discharged between August 2022 and May 2023 from the

Mbale Regional Referral Hospital Paediatrics Ward. This study was approved by the institutional review board at Nationwide Children's Hospital, USA and the Mbale Regional Referral Hospital Research Ethics Committee, Mbale, Uganda. A detailed description of the setting of this study and the available resources at the facility is available in a previous publication [14].

Pre-intervention

The baseline assessment demonstrated 3% overall adherence with deficits in almost all aspects of the guidelines [14]. Baseline findings were presented to key hospital stakeholders and care providers to develop initial quality improvement interventions. Several recommendations were produced. The greatest concerns identified in the baseline assessment were poor adherence to diagnostic testing recommendations and inadequate anti-malarial administration. It was determined that these areas should be the initial areas of focus for improvement interventions.

Interventions

Immediately following the presentation of the baseline assessment in April 2022, workflow changes were proposed and implemented. This involved standardizing the process of obtaining patient blood samples for thick and thin smears by the healthcare provider upon admission. This ensured confirmation of malaria diagnosis once the laboratory opened, even if the patient was admitted overnight. This change was facilitated by introducing the new policy at a departmental education session with the clinical staff who would be performing the testing. The clinicians who perform admissions were educated on the issue of delayed or absent diagnostic testing, and informed that the standard for the ward would be that they should obtain samples for testing themselves at the time of admission rather than writing the order for nursing staff to complete this at a later time. It was also proposed to utilize patient caregivers to assist in timing medications by informing them during ward rounds how many doses of anti-malarials were remaining for the child and the times those doses should be administered. The goal of this was to allow for better caregiver advocacy for drug administration and to assist nursing staff in timing medications accurately. This change to practice was also introduced at the same departmental education session with the ward clinicians. Efforts to improve documentation were also made, including use of a standardized patient chart.

In August 2022, an admission checklist sticker was introduced, also focused on improving rates of malaria diagnostic testing and artesunate administration (Fig. 1).

SUSPECTED SEVERE MALARIA

Admit date/time _____

Part 1: Testing

RDT Results _____

And/Or

BS Results _____

Part 2: Treatment

Artesunate #1 date/time _____

Artesunate #2 date/time _____

Artesunate #3 date/time _____

Fig. 1 Admission checklist sticker introduced in August 2022

The checklist was intended to be placed on the front of patient charts for children suspected of having severe malaria at the time of admission. The suspicion of severe malaria was at the discretion of the admitting clinician, and the ward was supplied with checklist stickers in all admitting areas. The sticker is bright yellow in color to grab attention, signaling to the treatment team a patient with likely severe malaria. The checklist includes confirmation of diagnostic testing and space to document its results. Additionally, the checklist emphasizes the timing for administration of the three minimum doses of artesunate. The checklist sticker was introduced at a departmental education session with clinical staff and teaching on its use was reviewed with any new clinical team members who started at a later date by study team leaders.

Data collection and analysis

The sample was selected on review of paper charts of children who had been discharged from the paediatrics ward between August 2022 and May 2023. This time period was selected to collect data after all of the interventions had been implemented (August 2022) and covering one year from the start of interventions (April 2022) with the intention that this data represent the results of the first intervention cycle of this quality improvement initiative. May 2023 was also selected as the ending time point due to the ability of the primary investigator to be present on site to finalize data collection at that time. After paediatric patients are discharged, their paper charts are archived in the Records Department. Discharged patient's charts available at the time of the study were assessed, and those with a clinician diagnosis of severe malaria were further reviewed. Upon review, 230 children met the WHO criteria for severe malaria (Table 1) [4–6].

Those that were excluded did not have documentation of any of the criteria used by the WHO to define severe

malaria in children. There were no additional exclusion criteria. Data were collected via manual chart review using a standardized case report form. Demographics, symptoms, laboratory results, treatments, length of stay, and mortality were extracted. Comparison of treatments received to standards as recommended in the WHO and Uganda Ministry of Health guidelines (Table 2) was undertaken [4–6].

The primary outcome measure was the proportion of patients receiving care consistent with all aspects of the WHO guidelines (Complete Adherence). Secondary outcome measures included the proportion of patients receiving each component of the WHO guidelines, the completion of an appropriate malaria diagnostic test, the proportion of patients receiving at least 3 doses of artesunate, and the timing of artesunate doses. All-cause and malaria-related mortality (death of a child who was diagnosed with malaria) were also reviewed. Adherence to guidelines was assessed for each patient both as a whole and for each guideline individually as it applied to that patient. The specific criteria used to determine adherence to each component of the guidelines has been described in a previous publication [14].

Analyses compare the baseline cohort (before all interventions) to the post-intervention cohort (after all interventions). Comparisons between groups were analysed using Chi-square or Fisher's exact test for categorical variables and Mann–Whitney test for continuous variables. Statistical analyses were conducted using GraphPad PRISM 9.0 (Boston, MA). Data are presented as median [interquartile range] unless otherwise specified. P value < 0.05 was considered significant throughout. Data concerning all-cause and malaria-related mortality were collected from

Table 1 Summary of WHO defining criteria for severe malaria

| Confirmed Malaria Parasitemia + Any of the Following |
|---|
| Altered mental status |
| Prostration |
| More than two seizures in 24 h |
| Metabolic acidosis with a base deficit of > 8 mEq/L or plasma bicarbonate < 15 mmol/L |
| Plasma lactate ≥ 5 mmol/L |
| Respiratory distress |
| Blood or plasma glucose < 40 mg/dL |
| Haemoglobin ≤ 5 g/dL or haematocrit ≤ 15%, |
| Haemoglobinuria |
| Serum creatinine > 3 mg/dL or blood urea > 20 mmol/L, |
| Plasma or serum bilirubin > 3 mg/dL |
| Clinical or radiographic evidence of pulmonary edema |
| Significant abnormal bleeding |
| Capillary refill ≥ 3 s or systolic blood pressure < 50 mmHg |

Table 2 Summary of WHO and Uganda ministry of health guidelines for management of severe malaria in children**Recommendations for all patients with severe malaria***Laboratory evaluation*

- Thick and thin blood films or rapid diagnostic test to confirm diagnosis of malaria
- Haemoglobin or haematocrit
- Blood glucose level
- Blood culture if feasible

General management

- Admit patients to highest level of care available
- Minimum 3 doses IV artesunate at admission, 12 h, and 24 h
3 mg/kg for children < 20 kg, 2.4 mg/kg for children ≥ 20 kg
- Following the parenteral course, patients should complete a full 3-day oral antimalarial course
- Empiric treatment for likely bacterial co-infection with broad-spectrum antibiotics
- If bacterial co-infection cannot be ruled out by blood culture/CSF analysis, complete an empiric course
- Correct dehydration and monitor urine output
- Administer paracetamol to maintain core temperature < 39C

Recommendations for patients with altered mental status

- Provide oxygen
- Assess for and correct hypoglycaemia if present with 5 ml/kg of 10% dextrose
- Insert nasogastric tube to prevent aspiration
- Position in lateral or semi-prone position and turn every 2 h
- If concerns for increased intracranial pressure, position supine with head raised about 30°
- Perform analysis of CSF

Recommendations for patients with seizure activity

- Provide oxygen
- Assess for and correct hypoglycaemia if present with 5 ml/kg of 10% dextrose
- Treat seizures with IV or rectal diazepam up to 2 doses 10 min apart
- If seizures persist, load with phenytoin or phenobarbital

Recommendations for patients with severe anaemia

- Provide oxygen
- Give blood transfusions to correct severe anaemia
10 ml/kg of packed red blood cells or 20 ml/kg of whole blood

Recommendations for Patients with Poor Perfusion

- Provide Oxygen
- Assess for anaemia and give blood transfusion if appropriate
10 ml/kg of packed red blood cells or 20 ml/kg of whole blood
- Assess for and correct dehydration and monitor urine output

the paediatrics ward registers and reported as monthly percent of total admissions or malaria admissions, respectively. These percentages were plotted over time in control charts constructed using healthcare rules in QI Macros for Excel (Denver, CO).

Results

Patients discharged after all interventions (post-intervention group) were compared to patients in the baseline assessment. There were 230 patients in the post-intervention group who were included, 58% of whom were male. The median age was 5 years (IQR 3–7.75 years). These characteristics did not differ significantly from those of the patients in the baseline assessment. Table 3 shows overall patient characteristics of the baseline and the

post-intervention patient populations. Median hospital length of stay for both groups was 3 days (IQR 2–4 days), and the mortality rate was 27% (n=40) in the baseline group and 19% (n=43) in the post-intervention group.

Complete adherence to severe malaria guidelines was achieved in 10% (n=23) of patients reviewed in the post-intervention group compared to 3% in the baseline group (p=0.007). There was also improvement in malaria diagnostic testing, up to 85% in the post-intervention group compared to 66% in the baseline group (p<0.0001) (Fig. 2). Other areas of improvement included haemoglobin monitoring, appropriate use of blood transfusions, and hypoglycaemia management (Fig. 2). There was an increased proportion of patients with appropriate overall artesunate administration (eligible patients who received

Table 3 Characteristics of the baseline population and post-intervention population

| Characteristic | Baseline (n = 147) | Post-intervention (n = 230) | P |
|--|--------------------|-----------------------------|------|
| Sex, n (%) | | | |
| Male | 81 (55%) | 134 (58%) | 0.9 |
| Female | 56 (38%) | 84 (37%) | |
| Unknown | 10 (7%) | 12 (5%) | |
| Age, years | 5 [2, 7] | 5 [3, 7.75] | 0.2 |
| Days of symptoms prior to presentation | 3 [2, 4] | 3 [2, 3] | 0.5 |
| Length of hospital stay | 3 [2, 4] | 3 [2, 4] | 0.6 |
| Discharge as deceased, n (%) | 40 (27%) | 43 (19%) | 0.06 |

the 3 minimum doses and the doses were given at an interval of 12 h ± 1 h, but this increase was not statistically significant (Fig. 2).

While this deficiency remains the greatest area of concern, the composite measure that requires all doses of

artesunate for which the patient is eligible be received and given on time fails to capture improvements seen in some aspects of artesunate administration. When evaluating the administration of each dose individually, improvements become apparent. In both groups, >90%

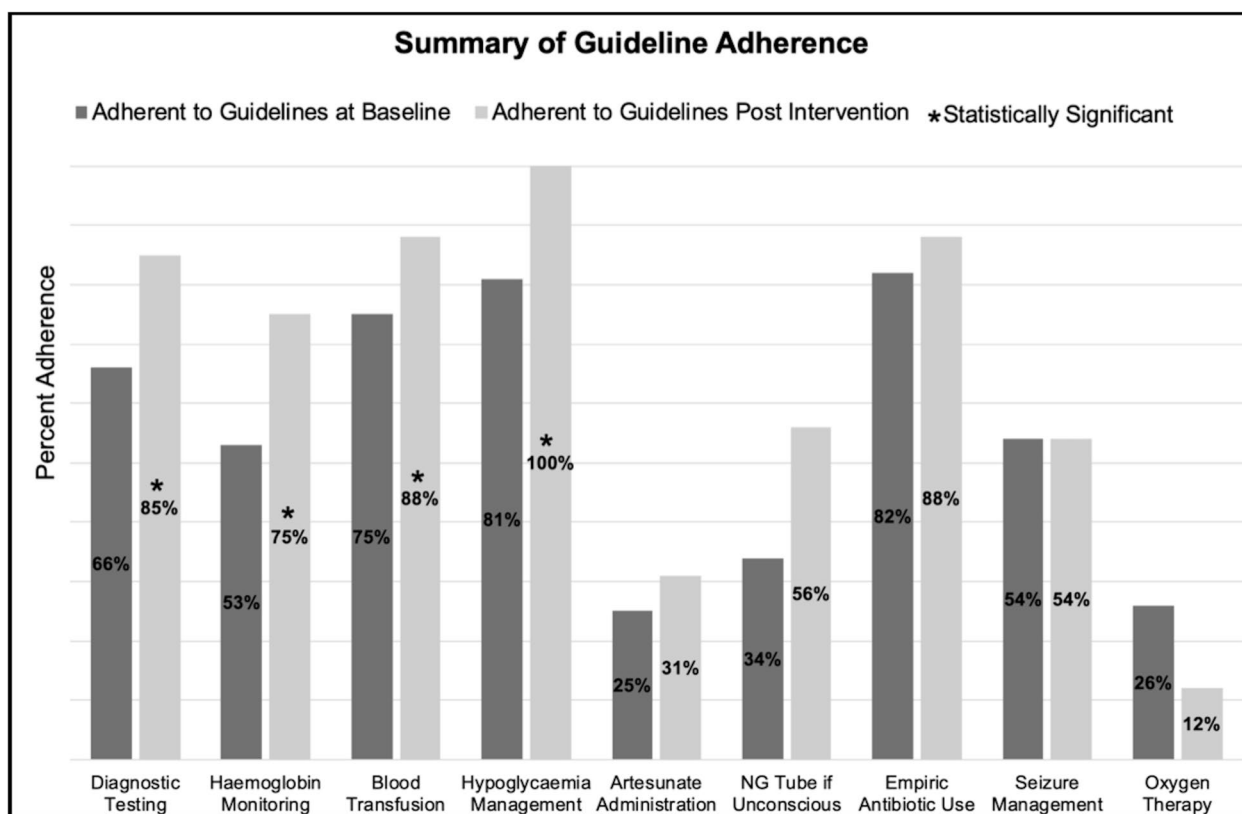


Fig. 2 Summary of adherence to treatment guidelines in children with severe malaria Each individual guideline adherence is presented for the subgroup of patients for which it was applicable. The number of patients included in each individual guideline assessment and p values for comparisons are as follows: Diagnostic Testing—baseline N = 147, post-intervention N = 230, p < 0.0001; Haemoglobin Monitoring—baseline N = 147, post-intervention N = 230, p < 0.0001; Appropriate Blood Transfusions – baseline N = 116, post-intervention N = 123, p = 0.01; Hypoglycaemia Management—baseline N = 48, post-intervention N = 27, p = 0.02; Overall Artesunate Administration—baseline N = 147, post-intervention N = 230, p = 0.2; NG Tube Use in Unconscious Patients—baseline N = 35, post-intervention N = 16, p = 0.2; Empiric Antibiotic Use—baseline N = 147, post-intervention N = 230, p = 0.1; Seizure Management—baseline N = 28, post-intervention N = 26, p > 0.99; Oxygen Therapy—baseline N = 95, post-intervention N = 150, p = 0.006

of patients received at least one dose of artesunate (baseline N=144, post-intervention N=218). There was a statistically significant increase in the proportion of eligible patients who received at least 3 doses and the percent of eligible patients receiving artesunate doses on time (Fig. 3).

While the recommended time between doses is 12 h, the median interval between dose one and dose two was 13.8 h in the post-intervention group (IQR 12.1–19.3 h) compared to a median of 14.9 h (IQR 12.4–20.3 h) in the baseline group (p=0.1). Similarly, there was an improvement in the median interval from dose two to dose three in the post-intervention group at 14.3 (IQR 12.3–24 h) compared to the baseline group at 16.8 h (IQR 13.7–25.1 h) (p=0.03). As was seen with overall artesunate administration, there was an increase in the proportion of unconscious patients who had appropriate use of nasogastric tubes, but this increase was not statistically significant. Areas of the guidelines in which there was

no improvement identified included empiric antibiotic use, seizure management, and the use of oxygen therapy (Fig. 2).

Malaria-related mortality rates (death in children who were diagnosed with malaria) over the course of the study period are shown in a control chart in Fig. 4. This rate is relative to all children with malaria, not only the severe cases that were the focus of the study interventions. Malaria-related mortality is seen to decrease over the study period until April 2023, at which time it rose again. All-cause mortality rates are shown in a control chart in Fig. 5, and are seen to decrease over the study period. These changes were not statistically significant when comparing pre- and post-intervention rates (malaria-related mortality p=0.7, all-cause mortality p=0.2). The all-cause mortality demonstrated a decrease in the mean rate (centre line shift downward) starting in February 2023 (Fig. 5).

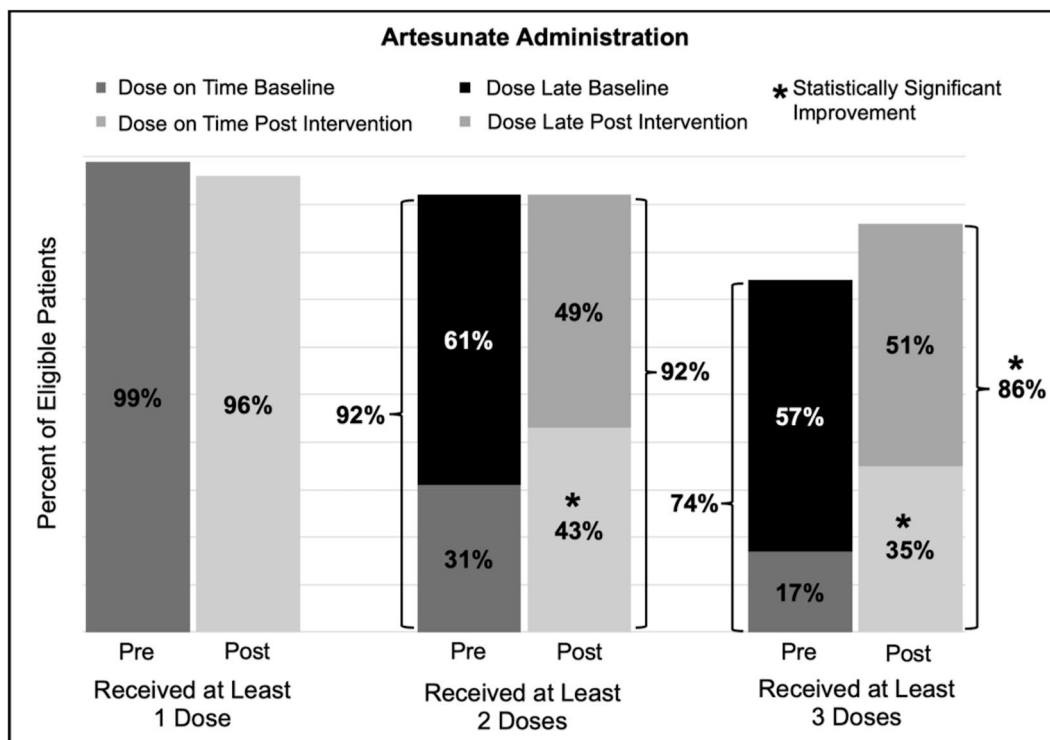


Fig. 3 Details of artesunate administration in the baseline and post-intervention groups. Results are reported as percent of patients who were still admitted and eligible to receive the next dose of artesunate. The number of patients included in each group and p values for comparisons are as follows: Received at Least 1 Dose—baseline N=146, post-intervention N=228; Received at Least 2 Doses—baseline N=127, post-intervention N=209, proportion of doses received on time p=0.02; Received at Least 3 Doses – baseline N=124, post-intervention N=201, proportion of doses received on time p=0.0003, proportion receiving 3 doses p=0.008

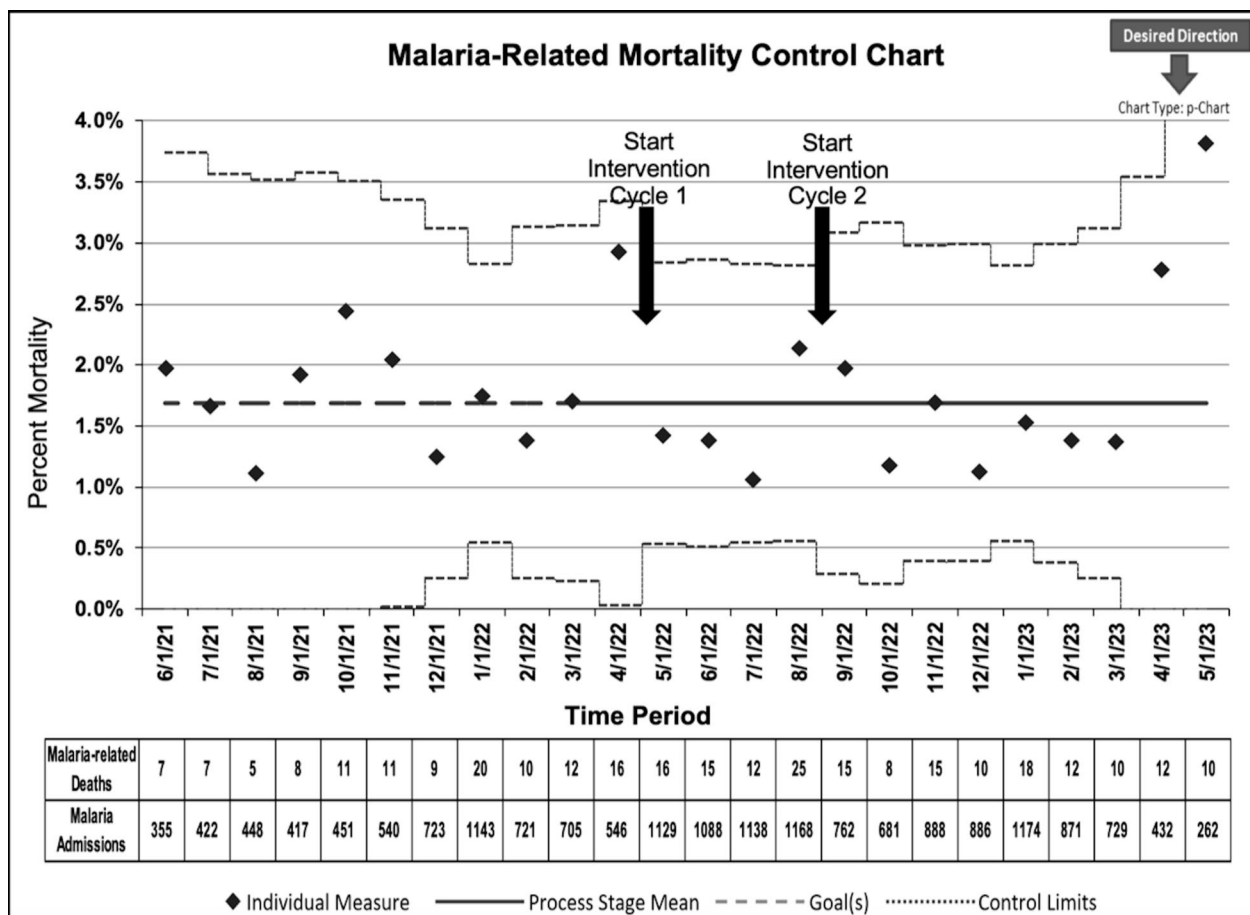


Fig. 4 Control chart of monthly malaria-related mortality rate

Discussion

This study sought to evaluate the impact of targeted interventions on the level of adherence to severe malaria treatment guidelines for children at Mbale Regional Referral Hospital in Eastern Uganda after the first intervention cycle of a quality improvement initiative. Overall adherence increased from 3% in the baseline assessment to 10% in the post-intervention period. There was particular improvement in malaria diagnostic testing and artesunate administration, which were the primary areas of focus for the interventions that had been implemented. The focus on these areas is in keeping with other studies in similar settings that have also identified malaria diagnostic testing and/or anti-malarial administration to be the most meaningful weaknesses in guideline adherence [15–18].

Treating providers noted that in the baseline assessment there were likely cases where malaria diagnostic testing was done, but results were not well documented.

It is probable that some of the improvement seen in diagnostic testing is related to improved documentation, which may have been helped by the use of the checklist sticker. At the time of the study, the patient charts were the only record of testing results and there was no independent record of malaria diagnostic testing to confirm or refute that these changes were related to documentation vs true increase in testing. It is possible that some of the other improvements observed are also related to documentation improvements. While the intention of the interventions undertaken in this study was to change clinical practice rather than documentation, improved documentation is still valuable to the treatment team and is crucial to allow for measurement and further improvement in the future. Other studies in similar settings have also noted documentation issues contributing to difficult data collection, and discrepancies in recording testing results playing a role in the observed low testing rates [17].

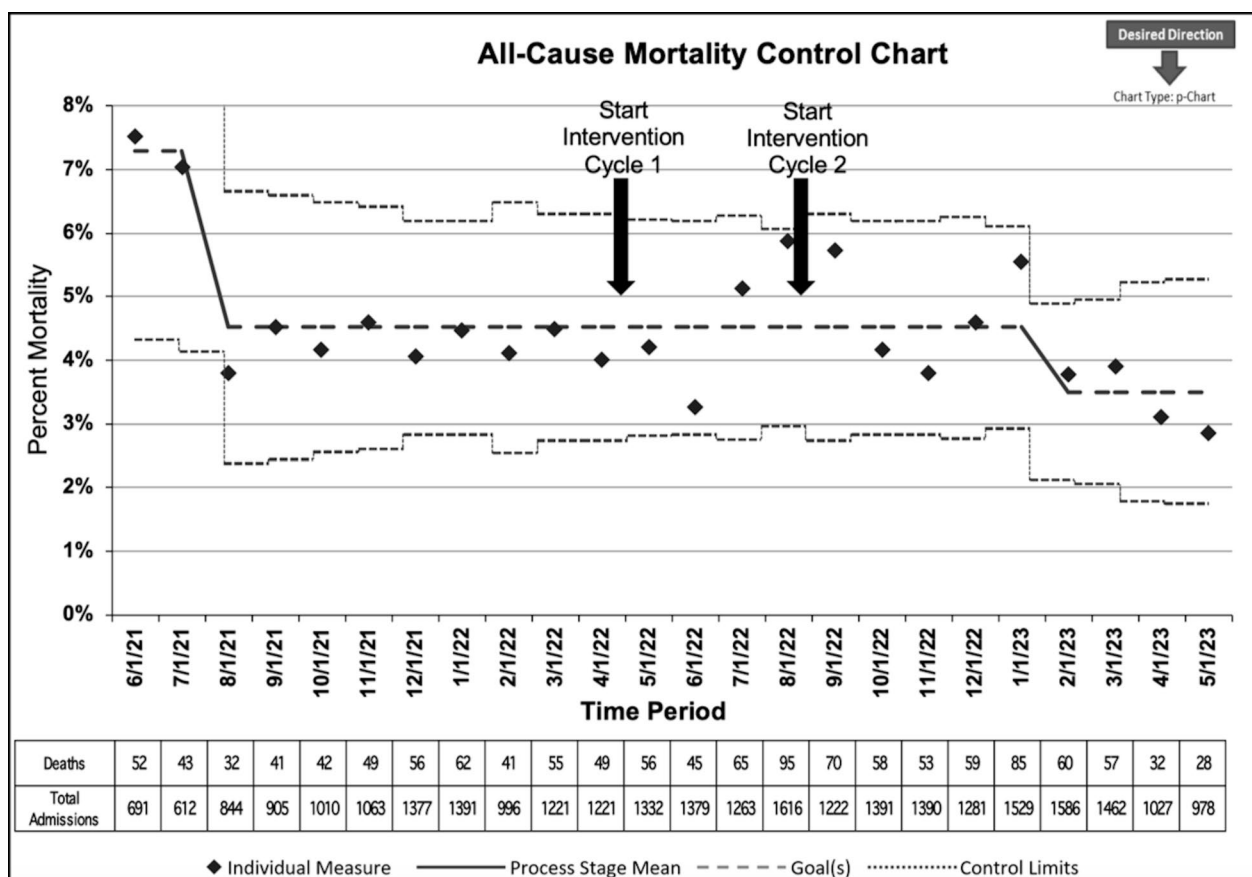


Fig. 5 Control chart of monthly all-cause mortality rate

While adequate artesunate administration remains a challenge, there was improvement in the number of patients who received three doses and the proportion of doses given on time. There was also an improvement in the median time between doses, though still falling short of the recommended 12-h interval. While there are no specific studies demonstrating that dosing at the 12-h interval directly improves outcomes, it has been shown that artesunate is rapidly cleared and active levels are nearly undetectable by 8 h after a dose is given [19]. This suggests that dose timing is a meaningful metric to follow and refine. Future improvement in these areas remains a priority, and greater uptake of the admission checklist sticker may help increase adherence.

To further improve malaria diagnostic testing beyond what has been achieved with these interventions, it is likely that supply issues will need to be addressed. Increased supplies of rapid diagnostic tests would allow for more consistent testing prior to anti-malarial treatment. It has been shown in several prior studies that adherence to the “test and treat” strategy recommended by the WHO is heavily impacted by the availability of

testing [5, 20–24]. Similarly, to further improve timely administration of medications, improved nursing ratios and adequate artesunate supply are necessary. Increased nursing staffing would also allow for closer monitoring of patient status. In one multi-country study, insufficient nursing staffing was universally noted by site leaders to be a contributor to poor guideline adherence [18]. Improvement in these areas is critical to improving patient outcomes due to the natural history of unmanaged malaria. Delays in malaria treatment lead to progression to more severe forms of disease, decreasing the likelihood of full recovery [25]. Furthermore, the inadequate administration or inappropriate use of artesunate may contribute to evolving drug resistance, which is increasing and likely to impact outcomes of future patients [1, 26].

Despite the resource limitations that are known to be present at this facility, many improvements were still possible by adapting interventions to the existing environment. While inadequate supply of glucometer test strips often limits testing for hypoglycaemia, improvement was achieved by focusing on the empiric administration of 10% dextrose for patients with altered consciousness,

seizure activity, and poor oral intake. In the baseline assessment, treating providers acknowledged that placement of nasogastric tubes in patients with altered consciousness was poorly documented, so some of the improvement in that area was likely related to an effort to more consistently document this intervention. Likewise, providers reported in both the baseline assessment and this study that oxygen is often provided without being documented. These investigators believe that the worsening of adherence in the use of oxygen therapy may be related to this documentation trend, and hope to see improvement in this regard in future assessments.

This study has several limitations. First, there were country-wide systemic issues that may have affected data in the final two months of the study period. Beginning April 1st of 2023 there was a critical shortage of physicians due to the lack of funding for intern and resident doctors that did not resolve until August 2023. This likely affected care delivery and documentation in the paediatrics ward during that time, impacting the data obtained for April and May 2023. Additionally and significantly, this study is a retrospective review of a convenience sample, and therefore cannot be certain to be representative of all cases at this facility. It is certain that the sample described here does not include all cases of severe malaria during the study period, and the charts reviewed were those that were available, not a random sample. Therefore, bias is likely to be present in these data – though the direction of impact of that bias cannot be known.

Data quality was also dependent on the quality of documentation in the paper charts, which was incomplete or illegible in some cases. Based on 5–7% of charts having missing demographic data as indicated by the proportion of patients with unknown sex, there is almost certainly data missing that cannot be accounted for in this study. It was not possible for the study team to determine exactly how much or what data may be missing, as patient charts are mostly free-form notes. If a provider did not write something in the patient chart, it could not be assessed. It is possible that actual adherence may be higher than what is presented here if patients received additional interventions or had test results that were not documented in the reviewed records. Furthermore, the cause of the improvements that were seen cannot be conclusively attributed to the implemented interventions. It is possible that these improvements were made due to other factors, or that the trend towards improvement was already in process before the study interventions occurred. It is also possible, as mentioned above, that some of the improvements seen were documentation improvements rather than true changes in practice. It also remains true that the clinical significance of adherence to each component of

these guidelines is not known, but given that adherence to standardized treatment protocols has been shown to improve outcomes in previous studies, this data is still relevant.

This study is not able to determine definitively the impact of improving guideline adherence on outcomes due to the lack of available outcomes data for severe malaria cases at this facility. The closest available metric is monthly overall malaria-related mortality in the paediatrics ward, which includes uncomplicated malaria cases as well as severe cases, leading to the low mortality rates (1–3%) that were reported in Fig. 4. The inclusion of non-severe malaria admissions in this number makes it difficult to detect a change due to how low the rates were prior to the implementation of the interventions. Without a complete sample of all severe malaria cases, it is not possible to know the mortality rate of severe malaria in the paediatrics ward at this time. The samples that were reviewed both in the baseline assessment and this study suggest that the severe malaria-related mortality rate is quite high, and future assessments will include efforts to accurately measure this important outcome. While not statistically significant, there was a centre-line shift downward on the control chart for all-cause mortality. This may be related to an improvement in severe malaria-related mortality, or may represent an overall improvement in care delivery.

Despite the limitations, the data presented here have demonstrated that targeted interventions were able to improve adherence to treatment guidelines in children hospitalized with severe malaria. These interventions were low-cost and required no additional equipment in the wards or laboratory. This is an encouraging example for other similar centres, who may be able to implement interventions like the admission checklist sticker within their existing resources.

The malaria treatment quality improvement initiatives in the Paediatrics Wards at Mbale Regional Referral Hospital remain ongoing. This data provides feedback and increased awareness for the treatment team, which has allowed for increased vigilance in the areas of weakness and commendations for the improvements achieved to date. Future work will focus on improving uptake of the existing interventions and repeat assessments to determine evolving needs, as well as evaluation of the impact of interventions on outcomes measures.

Conclusions

Adherence to severe malaria treatment guidelines in children at this Ugandan regional referral hospital has improved after implementing low-cost, targeted interventions. These improvements were associated with the implementation of an admission checklist for patients

suspected of having severe malaria and adjustments to workflow. Given the significant impact of severe malaria on paediatric morbidity and mortality, the success of these interventions suggests that similar approaches could be beneficial in other healthcare centres facing similar challenges.

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Author contributions

CM designed the study, performed chart reviews, completed all data input, assisted with statistical analysis, and was a major contributor in writing the manuscript. PO assisted in study design and was a major contributor in writing the manuscript. JW was a major contributor in writing the manuscript. JA was a major contributor in writing the manuscript. JM performed statistical analysis and was a major contributor in writing the manuscript. NO assisted in study design and was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

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

Declarations

Ethics approval and consent to participate

The Mbale Regional Referral Hospital Research Ethics Committee, Mbale, Uganda, approved this study March 16th, 2022. The Institutional Review Board at Nationwide Children's Hospital, USA, determined that this study is not research involving human subjects and waived the need for full approval.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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