SVOA Paediatrics

e-ISSN 2755-1660

ScienceVolks Open Access

Research Article

Clinical and Demographic Factors Influencing Treatment Response in Paediatric Malaria with Severe Acute Malnutrition (SAM)

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https://doi.org/10.58624/SVOAPD.2026.05.008

Received: April 27, 2026

Published: May 18, 2026

Citation: Abbas MM, Magzoub OS, Elhassn RS. Clinical and Demographic Factors Influencing Treatment Response in Paediatric Malaria with Severe Acute Malnutrition (SAM). *SVOA Paediatrics 2026*, 5:3, 61-70. doi: 10.58624/SVOAPD.2026.05.008

Abstract

Background: Severe Acute Malnutrition (SAM) and malaria remain leading causes of morbidity and mortality among children in sub-Saharan Africa. When combined, these conditions interact synergistically to worsen clinical outcomes.

Objectives: This study sought to: Identify demographic and clinical predictors of therapeutic response in severely malnourished children diagnosed with malaria. 2. Compare the effectiveness of commonly used antimalarial treatment regimens in this high-risk population. 3. Assess whether different forms of malnutrition (wasting, oedema, or a combination of both) influence treatment outcomes.

Methods: A hospital-based cohort of 96 children aged 6 months to 3 years admitted with malaria and coexisting severe acute malnutrition was analysed. Nutritional status was classified as oedematous, wasted, or mixed (oedema and wasting). Demographic characteristics, clinical features, and treatment modalities were retrieved from clinical records. Associations with treatment outcomes were evaluated using chi-square tests; $p<0.05$ was considered statistically significant.

Results: The sample included slightly more males (52.1%) than females, and most children (91.7%) originated from rural areas. Mixed malnutrition was the most prevalent presentation (68.8%). Overall treatment success was high (95.8%), with significantly better outcomes observed among males ($p = 0.049$) and rural residents (97.7% vs. 75.0%, $p = 0.034$). Artemisinin-based therapies demonstrated superior effectiveness: Co-artem achieved a 100% response rate, and Artesunate yielded 97.1%, compared with 92.3% for Quinine. Notably, none of the children treated with Artemether showed a good therapeutic response ($p<0.001$). Clinical recovery was unaffected by mid-upper arm circumference or nutritional status category, with no statistically significant differences observed ($p>0.05$).

Conclusion: In this rural cohort of young children with severe acute malnutrition, artemisinin-based combination therapies, particularly artemether–lumefantrine, showed excellent efficacy, whereas artemether monotherapy failed. These findings underscore the urgent need to discontinue monotherapies and reinforce adherence to WHO treatment guidelines.

Keywords: *Malaria, Severe Acute Malnutrition, Demographic Features, Treatment Outcomes.*

Introduction

Malaria and malnutrition are major contributors to childhood mortality in endemic regions, particularly in sub-Saharan Africa. They frequently coexist, with each condition worsening the other: malaria can aggravate nutritional deficits, while undernutrition increases susceptibility to severe malaria. Young children are especially vulnerable, and the risk is further amplified by low socio-economic status, which predisposes families to both malnutrition and infection [1]. Concurrently, severe acute malnutrition is a critical risk factor, directly contributing to nearly half of all deaths from infectious diseases in this age group by compromising immune competence and physiological resilience [2].

The confluence of malaria and severe acute malnutrition creates a vicious cycle of worsened outcomes. The pathophysiological alterations caused by severe acute malnutrition, including impaired immune function, metabolic dysregulation, and potential changes in drug pharmacokinetics, can exacerbate the severity of malaria and potentially compromise the efficacy of antimalarial treatments [3, 4]. A clear understanding of the bidirectional relationship between malaria and malnutrition is critical, given their substantial global burden. While the negative impact of malaria on linear growth and weight gain in children is well established, the extent to which pre-existing undernutrition modifies malaria susceptibility and clinical outcomes remains incompletely defined and has been a topic of scientific debate since the 1950s [5].

Parenteral artesunate has demonstrated clear survival benefits in two major clinical trials, outperforming parenteral quinine, the longstanding standard of care. In contrast, quinine administration is logistically challenging, requiring frequent intravenous infusions or intramuscular dosing, and is associated with significant adverse effects, including hyperinsulinaemic hypoglycaemia and neuro-ocular toxicity. Consequently, artesunate offers not only superior efficacy but also significant advantages in safety, ease of administration, and reduced workload for healthcare providers [6].

In 2006, the World Health Organization designated artemisinin-based combination therapies (ACTs) as the global first-line treatment for *Plasmodium falciparum* malaria. The portfolio of WHO-recommended ACTs now includes six combinations, most recently artesunate–pyronaridine. When integrated with large-scale distribution of insecticide-treated nets and chemoprevention programs, the widespread adoption of ACTs has been central to the marked reductions in malaria incidence and mortality observed over the past decade, particularly in sub-Saharan Africa. [7].

This study investigated severely malnourished children with malaria to define predictors of treatment success, assess the effectiveness of commonly used antimalarial regimens, and evaluate the influence of malnutrition phenotypes on clinical outcomes.

Methodology

Study Design and Duration:

This was an observational, analytical, hospital-based cohort study. The study was conducted from April 2021 to January 2022. The design involved enrolling a cohort of paediatric patients with Severe Acute Malnutrition (SAM) and malaria at admission and following them to assess their response to treatment.

Study Area:

The study was conducted in the dedicated malnutrition wards of two major pediatric teaching hospitals in Omdurman, Sudan: Mohammed Alamin Hamid Pediatric Hospital and Al Buluk Teaching Hospital. These centres are key referral hospitals with specialized nutritional support programs, intensive care units (PICU/NICU), and complete laboratory facilities, serving a diverse population from Khartoum and other states across Sudan. This setting provided a robust environment for studying this specific patient cohort.

Study Population and Eligibility Criteria:

The study population comprised paediatric patients diagnosed with both Severe Acute Malnutrition (SAM) and laboratory-confirmed malaria.

Inclusion Criteria:

Children admitted with a diagnosis of SAM:

* Laboratory-confirmed diagnosis of malaria.
* Admitted to the malnutrition wards of either study hospital during the study period.
* Patients of all ages and both genders were included.
* Written informed consent provided by a parent or guardian.

Exclusion Criteria:

* Parents or guardians who refused to participate in the study.

Sampling and Sample Size:

A total coverage (census) sampling method was employed because the number of cases with both SAM and malaria was relatively limited during the study period. All eligible patients who presented to the study sites and met the inclusion criteria were enrolled. The final study cohort consisted of 96 participants.

Data Collection Tools and Methods

Data were collected using a combination of patient records and a specially designed, researcher-administered questionnaire. Strict COVID-19 prevention protocols, including the use of face masks and disposable gloves, were followed during all patient interactions.

The data collection process captured the following:

1. Baseline Socio-demographic and Clinical Data: Extracted from patient records, including age, gender, residence, and detailed clinical presentation upon admission.

2. Anthropometric Measurements: Conducted at admission by the researcher (a 4th-year paediatric registrar) using standardized hospital equipment to confirm nutritional status.

* Weight: Measured in kilograms using a standard hospital balance scale.
* Height/Length: Measured in centimetres using a standard tape.

3. Treatment and Outcome Data:

* Treatment Regimen: Data on the specific antimalarial and nutritional support therapies administered were recorded from patient charts.
* Treatment Response Parameters: Outcome measures were defined and collected, which may have included time to fever clearance, parasite clearance time, length of hospital stay, and anthropometric improvement during hospitalization.

4. Laboratory Investigations: Data on malaria parasite burden and relevant haematological parameters (e.g., haemoglobin for anaemia) were extracted from laboratory reports to monitor biological response.

Study Variables:

* Independent Variables (Potential Influencing Factors): Age, gender, residence, baseline clinical presentation, and nutritional status (anthropometric measurements).
* Dependent Variables (Measures of Treatment Response): Defined outcome parameters such as parasite clearance, clinical recovery, and length of hospital stay.

Data Management and Statistical Analysis:

Data were entered and analyzed using the Statistical Package for the Social Sciences (SPSS), version 23. Descriptive statistics (frequencies, means/medians) were used to summarize the cohort's characteristics. Analytical statistics were applied to identify factors influencing treatment response. The Chi-squared test was used to assess associations between categorical independent variables and treatment outcomes. A p-value of less than 0.05 at a 95% confidence level was considered statistically significant. Results were presented using cross-tabulations, tables, and graphs.

Results

Patient Demographics:

A total of 96 pediatric patients were included. Slightly more than half were male (52.1%), while 47.9% were female. Ages ranged from 6 months to 3 years, with a mean of 14 months (SD = 4.6). The most significant proportion of patients (43.8%) were aged 12–<18 months, followed by those 6–<12 months (34.4%), and 18–<24 months (18.8%) (Figure 1). Rural residents constituted the vast majority of the cohort (91.7%), whereas only 8.3% of the children came from urban areas.

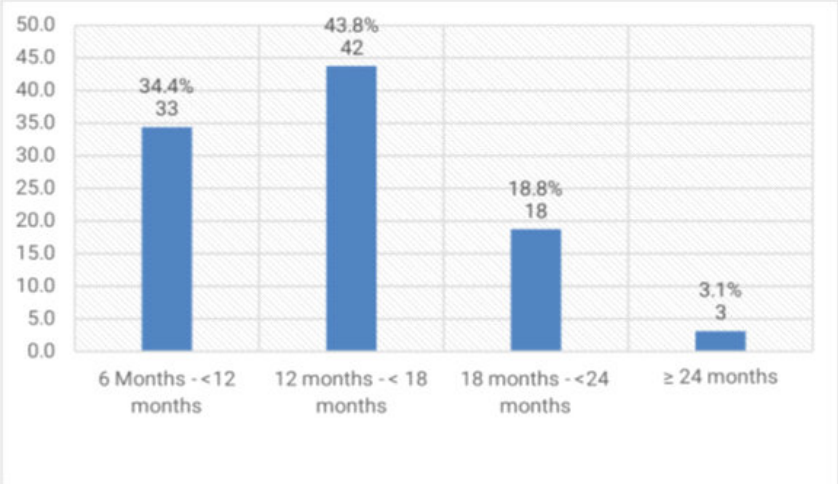

Figure 1. Age distribution of the participants in years (n=96.

Clinical Characteristics:

With respect to nutritional classification, 7.3% presented with kwashiorkor, 24% with marasmus, and 68.8% exhibited mixed edema and wasting (Figure 2). For the majority (85.4%), the current episode was their first documented malaria episode, whereas 14.6% reported prior episodes. Fever was a universal presenting symptom across the cohort.

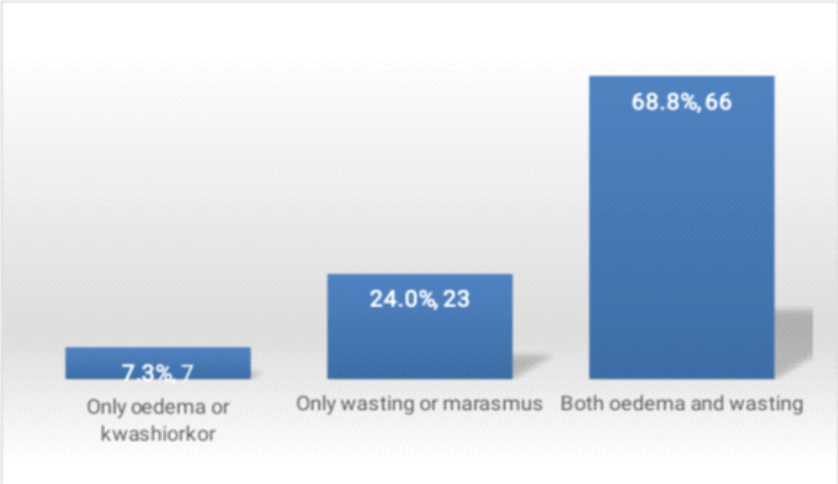

Figure 2. The admission criteria of the participants (n=96).

Clinical Examination Findings:

Markers of severe acute malnutrition were prominent. More than half of the children (56.3%) had a mid-upper-arm circumference (MUAC) <11.5 cm, and 43.8% had MUAC values between 11.5 and 12.5 cm (Figure 3). Consistently, 69.8% demonstrated a weight-for-height/length Z-score of −3, while 30.2% had a Z-score of −2 (Figure 4).

Vital signs at admission showed that 64.6% were normothermic, whereas 35.4% remained febrile. The pulse rate was normal in 85.7%, and 2.2% exhibited tachycardia. The respiratory rate was normal in 80.7%, and 3.4% presented with tachypnea (Figure 5).

On systemic examination, splenomegaly was the most prevalent finding (80.9%), followed by hepatomegaly (39.7%) and peripheral edema (11.8%) (Table 1).

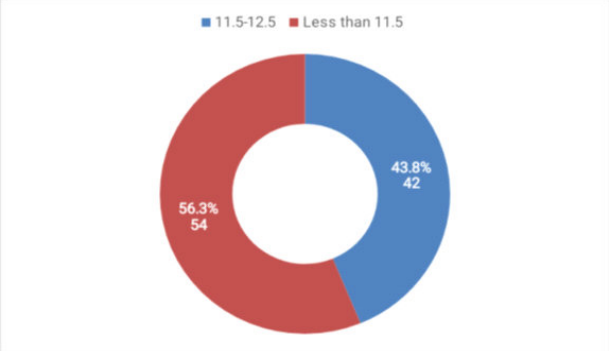

Figure 3. The mid-upper-arm circumference among the participants (n=96).

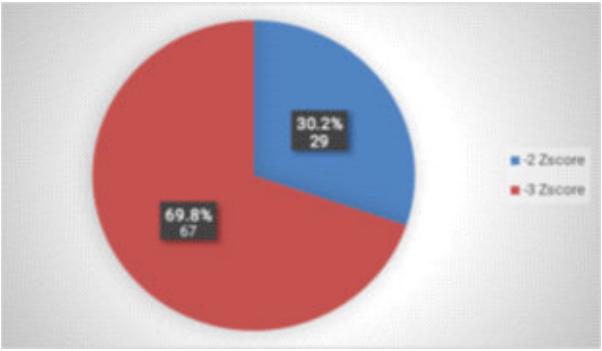

Figure 4. The Weight-for-height/length among the participants (n=96).

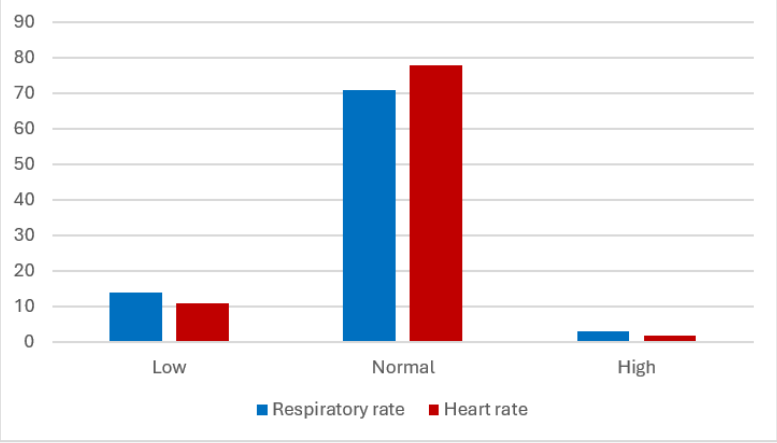

Figure 5. Respiratory and heart rates of the participants (n=96).

Table 1. The clinical presentation of the participants (n=96).

Clinical Sign	Present % (n)	Absent % (n)
Fever	100.0% (96)	0.0% (0)
Pallor	96.9% (93)	3.1% (3)
Splenomegaly	80.9% (78)	19.1% (18)
Hepatomegaly	39.7% (38)	60.3% (58)
Hypoglycemia	15.6% (15)	84.4% (81)
Impaired consciousness/prostration	14.6% (14)	85.4% (82)
Peripheral edema	11.8% (11)	88.2% (85)
Convulsion	6.3% (6)	93.8% (90)
Shortness of breath	3.1% (3)	96.9% (93)
Jaundice	1.0% (1)	99.0% (95)
Altered level of consciousness	1.0% (1)	99.0% (95)

Treatment and Clinical Outcomes:

Antimalarial treatment varied within the cohort: 47.9% received Co-artem, 36.5% received Artesunate, and smaller proportions received other regimens. Clinical outcomes were overwhelmingly favorable. A good response to therapy was observed in 95.8% of patients, whereas 4.2% demonstrated a partial response. Similarly, 95.8% were classified as clinically cured, and 4.2% were partially cured at discharge.

Associations Between Clinical Variables and Treatment Response:

Significant associations emerged between treatment response and selected demographic variables. Male sex was associated with a higher rate of good response ($p = 0.049$) (Table 2). Residence also demonstrated a significant association ($p = 0.034$), with 97.7% of rural patients showing a good response compared with 75% of urban patients.

Table 2. The association between the response to treatment and the Sex of the patients (n=96).

		Sex		P value Fisher's Exact Test
		Male	Female	
Response to treatment	Good	100.0%(50)	_91.3%(42)	.049
	Partial response	0.0%(0)	8.7%(4)	
Total		100.0%(50)	100.0%(46)	

The strongest association was observed between treatment response and type of antimalarial therapy ($p < 0.001$). A good therapeutic response was observed in all patients treated with Co-artem (100%), in 97.1% of those receiving Artesunate, and in 92.3% of children treated with Quinine. In contrast, none of the patients who received Artemether monotherapy achieved a good response (Table 3).

In contrast, no statistically significant associations were observed between treatment response and MUAC ($p = 0.797$), weight-for-height/length Z-score ($p = 0.582$), or whether the current malaria episode was the first attack ($p = 0.627$).

Table 3. The association between the response to treatment and the management received by the patients(n=96).

		Management received				P value Fisher's Exact Test
		Coartem	Artemether	Artesunate	Quinine	
Response to treatment	Good	100.0%(46)	0.0%(0)	97.1%(34)	92.3%(12)	.000
	Partial response	0.0%(0)	100.0%(2)	2.9%(1)	7.7%(1)	
Total		100.0%(46)	100.0%(2)	100.0%(35)	100.0%(13)	

Discussion

This study provides a critical analysis of the clinical profile and treatment outcomes of malaria in a high-risk cohort of 96 pediatric patients with severe acute malnutrition (SAM). Our findings underscore the complex interplay between malnutrition and malaria, revealing a high burden of severe disease and excellent overall therapeutic success with artemisinin-based combination therapies (ACTs), while uncovering unexpected and significant variations in response to specific antimalarial regimens.

A key finding of our study is the overwhelming predominance of malarial manifestations in a predominantly rural (91.7%) and young (mean age 14 months) population. The high prevalence of SAM, with 69.8% of children exhibiting a weight-for-height Z-score of -3 and 56.3% having a mid-upper-arm circumference (MUAC) <11.5 cm, establishes this as a particularly vulnerable cohort. This aligns with the well-documented synergistic relationship between malnutrition and infectious disease burden.

Malnutrition increases susceptibility to infection and is frequently accompanied by recurrent and diverse infectious episodes, including bacterial, viral, and parasitic diseases, as well as chronic inflammation, reflecting an underlying impairment of immune function. Malnutrition-associated alterations in the intestinal microbiota and the presence of environmental enteric dysfunction are strongly linked to growth failure, disruption of both systemic and mucosal immunity, and persistent inflammatory responses. In turn, infection and inflammation further exacerbate nutritional deficits, creating a self-perpetuating vicious cycle that reinforces poor health outcomes [8]. Dietary deficiencies are central contributors to the burden of malaria and anemia. Deficits in essential micronutrients, including iron, folate, vitamin A, and zinc, impair immune competence, weaken host defence against infection, and disrupt erythropoiesis. In malaria-endemic settings characterized by food insecurity, poverty, and high infectious disease prevalence, undernutrition both drives and results from poor health, reinforcing disease susceptibility and severity [9]. The high prevalence of organomegaly observed in this cohort, particularly splenomegaly (80.9%), underscores its significance as a major contributor to massive splenic enlargement in malaria-endemic regions. Hyperreactive malarial splenomegaly (HMS) represents a key underlying etiology, arising from an exaggerated immune response induced by repeated or prolonged *Plasmodium* infections [10].

Despite the high acuity of illness suggested by the nutritional and clinical examination findings, the overall clinical outcome was remarkably positive, with 95.8% of patients achieving a good response and clinical cure. This success rate is a testament to the efficacy of modern antimalarial regimens, particularly ACTs, which are the cornerstone of malaria management in sub-Saharan Africa [11].

The finding that residence and sex were significantly associated with treatment response warrants careful interpretation. The higher reasonable response rate in rural versus urban patients (97.7% vs. 75%) may be influenced by unmeasured confounders such as health-seeking behavior, adherence to follow-up, or exposure to different malaria parasite strains. The association with male sex, while statistically significant, should be interpreted with caution due to the relatively small sample size and requires validation in larger studies.

The most striking and clinically significant finding of our analysis is the influential association between the specific antimalarial agent and treatment response ($p < 0.001$). We observed a 100% response rate in children treated with Co-artem (artemether-lumefantrine) and a 97.1% response rate in those receiving Artesunate. This is consistent with current WHO guidelines, which strongly recommend ACTs for the treatment of uncomplicated Plasmodium falciparum malaria. The high efficacy of Co-artem, the most widely used ACT, is well established across diverse settings, including in children with comorbidities [12].

However, the finding that none of the patients treated with Artemether monotherapy achieved a good response is alarming and merits serious consideration. Artemisinin resistance has emerged since 2008, attributed mainly to prolonged artesunate monotherapy use and circulation of substandard drugs. It is clinically defined by delayed parasite clearance (half-life ≥5 hours or day-3 parasitemia) and molecularly associated with mutations in the *kelch13* gene identified in 2014. Importantly, complete treatment failure to artemisinin has not yet been reported [13]. The poor response observed in our cohort could be indicative of sub-therapeutic dosing, poor absorption in the context of SAM, or, more worryingly, the emergence of partial artemisinin resistance. The delayed parasite clearance associated with artemisinin resistance has now been confirmed in multiple regions of Africa, including Rwanda, Uganda, and Eritrea [14, 15]. Our results highlight the critical importance of using artemisinin derivatives only in combination with a partner drug to ensure complete parasite clearance and prevent resistance. The continued use of monotherapies, even in hospital settings, represents a dangerous practice that must be urgently addressed.

It is noteworthy that we found no significant association between the degree of malnutrition (as measured by MUAC or WHZ) and antimalarial treatment response. This suggests that with appropriate, effective combination therapy, even profoundly malnourished children can clear parasitaemia and achieve clinical cure. This is an encouraging message for clinicians and reinforces the principle that SAM should not lead to therapeutic nihilism. The primary challenge in this population often shifts from curing the malaria infection itself to managing the complex metabolic and nutritional complications that coexist.

Limitations

Our study has several limitations, including an observational design that limits generalizability and the ability to establish causality. The sample size, particularly for sub-group analyses of specific antimalarials, was small. We did not have access to molecular data to confirm parasite species, quantify parasite density, or test for genetic markers of drug resistance, which would have been invaluable in interpreting the Artemether monotherapy failure.

Conclusion

In conclusion, this predominantly rural cohort of very young children with severe acute malnutrition, treatment outcomes were strongly influenced by both demographic factors, particularly sex and residential setting, and therapeutic regimen. Artemisinin-based combination therapies, especially artemether–lumefantrine, achieved excellent clinical efficacy, confirming their effectiveness in high-risk pediatric populations. Conversely, the failure of artemether monotherapy highlights the urgent need to discontinue non-combination regimens and to reinforce strict adherence to WHO treatment guidelines and pharmacovigilance to preserve antimalarial effectiveness.

Recommendations: Routine use of artemisinin-based combination therapies should be strictly enforced, with immediate cessation of all artemisinin monotherapies in clinical practice. Strengthening supply chain management to ensure uninterrupted access to quality-assured ACTs in rural and high-burden settings is essential. Enhanced pharmacovigilance and resistance surveillance, including molecular monitoring for *kelch13* mutations, should be integrated into national malaria control programs. Finally, coordinated care models that link malaria treatment with comprehensive management of severe acute malnutrition are recommended to optimize outcomes in this vulnerable pediatric population.

Despite the high acuity of illness suggested by the nutritional and clinical examination findings, the overall clinical outcome was remarkably positive, with 95.8% of patients achieving a good response and clinical cure. This success rate is a testament to the efficacy of modern antimalarial regimens, particularly ACTs, which are the cornerstone of malaria management in sub-Saharan Africa [11].

Ethical Considerations

Ethical approval was secured from the Sudan Medical Specialization Board (Council of Pediatric and Child Health), the Ministry of Health, and the participating hospital. The study goals were explained to all caregivers and participants. Written informed consent was obtained from caregivers, and voluntary assent was obtained from children aged 5 years or older. Strict COVID-19 infection prevention measures, including mask use, hand hygiene, and disposable gloves, were implemented throughout data collection.

Disclosure of Conflict of Interest

Nothing to disclose.

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