INITIAL CLINICAL PRESENTATION, DIAGNOSTIC EVALUATION AND EMERGENCY PROVIDER CLINICAL IMPRESSION OF FEBRILE CHILDREN LESS THAN FIVE YEARS OLD PRESENTING TO THE EMERGENCY MEDICINE DEPARTMENT AT MUHIMBILI NATIONAL HOSPITAL IN DAR ES SALAAM, TANZANIA.

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By

Faith Herman Ringo MD

A dissertation submitted in (partial) Fulfillment of the Requirements for the Degree of Master of Medicine (Emergency Medicine) of Muhimbili University of Health and Allied Sciences

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled: ***Initial clinical presentation, diagnostic evaluation and emergency provider clinical impression of febrile children less than five years old presenting to the emergency medicine department in Muhimbili National Hospital in Dar Es Salaam Tanzania*** in (Partial) fulfillment of the requirements for the degree of Master of Medicine (Emergency Medicine) of Muhimbili University of Health and Allied Sciences.



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I, **Faith Herman Ringo**, declare that this dissertation is my own original work and that it has not been presented and will not be presented to any other university for a similar or any other degree award.

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DEDICATION

To my parents, Mr. & Mrs. Herman Ringo and my beautiful and lovely daughters Angel and Ariana and my best friend Dr Hendry R. Sawe who have always felt proud and supported me through-out difficulties and happiness. God bless you always.

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LIST OF ABBREVIATIONS

MNH	-	Muhimbili National Hospital
MUHAS	-	Muhimbili University of Health and Allied Sciences
WHO	-	World Health Organization
EMD	-	Emergency Medical Department
CBC	-	Complete Blood Count
CSF	-	Cerebral Spinal Fluid
DPT.HB	-	Diphtheria pertussis, tetanus, hepatitis B
RDT	-	Rapid diagnostic test

ABSTRACT

BACKGROUND: Fever is one of the most common reasons for pediatric emergency department visits, accounting for as many as 20% of all presentations. A variety of diagnostic tests, including blood, urine and CSF testing, as well as chest radiography and pathogen-specific rapid diagnostic tests (RDT) may be useful in the evaluation of the febrile child and appropriate diagnostic testing may vary based on age and clinical presentations. While there are many published recommendations for the evaluation of febrile children less than five years old in the acute care setting, little is known about the actual diagnostic management and ultimate emergency provider clinical impression of febrile children less than five years old in limited-resource settings.

AIM OF STUDY: To describe the clinical presentations, diagnostic evaluation, treatment and emergency provider clinical impression of febrile children less than five years old at the MNH EMD in Dar Es Salaam, Tanzania.

METHODS: This was a observational descriptive study conducted from August through November 2012 at the MNH EMD, a tertiary care center with approximately 36,000 EMD visits per year. We enrolled a convenience sample of children less than five years old who presented with fever or reported fever. Treating physicians prospectively completed a standardized data collection form.

RESULTS: We enrolled 105 febrile children less than five years old in the study with the median age of 14 months. Sixty-four percent were male. Since Muhimbili is a tertiary referral hospital, the majority of the patients (54.3%) were referred. The predominant symptoms from this cohort of febrile children less than five years old were

poor feeding (47.6%) vomiting (42.9%), cough (34.3), difficulty in breathing (28.6%), diarrhea (22.9%), abdominal distension (14.3%), and convulsions (13.3%).

Seventy-eight percent had at least one vital sign abnormality, while 82% had an abnormal physical examination findings. Point-of care tests included random blood glucose on all children under 5 (100%), malaria RDT on 103 (98.1%), urine dipstick on 30 (28.6s%), rapid HIV test on 26 (24.80 %) and venous blood gases on 59 patients (56.19%). While in the EMD, most children less than five years old received at least one therapeutic treatment: 73 (70%) received at least one antibiotic, 13 (12%) received anti-malarial medication, 57 (54%) received intravenous fluids and 43 (41%) received an anti-pyretic. The top emergency physician clinical impressions are also reported.

CONCLUSION: In MNH EMD, a range of diagnostic tests are used to determine cause of fever though testing results do not always correspond with reported clinical impressions. In referred patients, administration of antipyretics, antibiotics, and anti-malarial prior to ED arrival was common. Bacterial infections were very common among children under 5 years who were tested.

RECOMMENDATIONS:

1) We recommend the development of a symptom-based diagnostic testing protocol to rationalize our approach to diagnosis and management of febrile children under 5 years.

2) We recommend execution of larger prospective study with definitive testing to further characterize the etiology of febrile illnesses in acute care settings in this region.

1.0 INTRODUCTION AND LITERATURE REVIEW

Fever is defined as elevated body temperature of or above 37.5°C axillary or 38°C rectally (1,2) Although tympanic and axillary temperature measurements are not as reliable in infants (3,4) axillary temperature is often the only method used in many settings. Fever is one of the most common reasons for pediatric emergency department visits, accounting for as many as 20% of all presentations, and is most commonly caused by an infectious process(3,5,6). Febrile illness is the leading cause of admissions in Africa and accounts for significant morbidity and mortality(7). Fever is not a diagnosis in and of itself, but a nonspecific response to systemic infection or inflammation(8). Infectious causes of fever include bacterial, viral, fungal, and parasitic illnesses, and viral etiologies remain the most common in children presenting to an emergency department setting for fever(1,3,9,10). Non-infectious causes of fever include tumors, trauma, and stress.

Fever can be a manifestation of a serious bacterial infection, such as meningitis, pneumonia, bone and joint infections, urinary tract infections, enteritis, and bacteremia (1,11,12). Bacterial infection, most notably pneumonia, is the major cause of death among children in the developing world and early identification of serious bacterial illnesses is imperative to reduce morbidity and mortality(13). In Tanzania, malaria is also a common and life threatening cause of fever in children, and febrile patients may be presumptively diagnosed with malaria even when rapid diagnostic testing or microscopy for parasites is negative. One study done in Tanzania found that malaria is over-diagnosed in children with fever, and untreated bacterial infections increased mortality in those misdiagnosed children (14).

Traditionally, the approach to fever in the pediatric population varies by age, and children are usually stratified into three subgroups: neonates (0-28 days), young infants (1-3 months), and older infants or toddlers (3-36 months of age). The assessment of fever in infants less that 3 months of age is a particular challenge due to frequent lack of localizing signs and their inability to articulate complaints, and this age group is most susceptible to occult bacterial infections (4)

While many young infants (<3months) may be well appearing at presentation, studies have demonstrated that there exists approximately a 9% incidence of severe bacterial infection in this population. Among this group, neonates (ages 0-28 days) are at increased risk of perinatal and community acquired infections, including but not limited to Group B *streptococcus*, *Listeria monocytogens*, *Streptococcus pneumonia*, *Haemophillus influenza*, *E. coli* and herpes simplex virus (16).

Studies in the United States have demonstrated that approximately 12-28% of febrile neonates presenting to the emergency department have serious bacterial infections, with the remaining having a non-specific viral illness(17). Typically these infants receive a full diagnostic work up including a CBC with differential and blood culture, CSF studies and culture, urine studies and culture, and radiographic imaging if indicated. Algorithms, such as the "Rochester criteria" are widely used in high-resource settings as a tool for identifying febrile infants at low risk for serious bacterial illnesses(18). In a 2005 study of bacteremia in children in rural Kenya, 12.8% of those <60 days old had bacteremia, with known isolates identified as Group B *Streptococcus* and *E. Coli* (19). Previous studies on infants ages 1-3 months have shown that these infants are at risk for Group B *streptococcus*, *Staph. aureus*, *Strep. pneumonia*, *Haemophillus influenza*, and

Neisseria meningitides, and bacteremia in this age group was noted in 5.9% of the study population, with isolates identified as *Streptococcus pneumonia*, non-typhoid *salmonellae*, *Haemophillus influenza* and *E. coli* (20).

A United States study looking at fever in children 1- 3 months of age utilized diagnostic tests including blood, urine and CSF studies, and chest radiograph to categorize patients into "high risk" and "low risk" groups(20). This stratification was then used to guide treatment. Subsequent investigations such as the Baker, et. al. study, which led to the creation of the "Philadelphia criteria", devised further treatment recommendations for low risk patients, going as far as providing recommendations on which patients could safely be treated on an outpatient basis(17) .

The Philadelphia criteria is based on interpretation of clinical presentation and laboratory and radiographic data. Baker et al. were able to demonstrate a negative predictive value of 99.7% for identifying serious bacterial infection.

With the introduction of the Prevnar vaccine against *Streptococcus* to the childhood immunization schedule in the United States (administered at 2, 4, and 6 months of age), the prevalence of SBI in febrile children decreased, and a less stringent strategy for the work up and treatment of febrile children older than 3 months of age presenting with fever is considered acceptable(2) . Typically, CSF studies are not recommended in this age group if the child is well appearing, and a clinician may even discharge patients home without antibiotics. In contrast, in studies from 12 different African countries, where streptococcal vaccines may not be available and access to healthcare is often limited, a much higher mortality rate of 20% is reported in febrile children under the age

of 5. This rate is likely high enough to require a conservative workup and admission strategy for most febrile children. Major causes of death include malaria (22%), acute respiratory infections (16%), diarrhea (14%), measles (8%), HIV (8%), and neonatal sepsis (13%) (8) many of which are uncommon and rarely fatal in high-resource settings (6).

One of the greatest challenges emergency physicians in sub-Saharan Africa face is the need to evaluate the relevance of pediatric fever risk stratifications from areas with a different disease burden and vaccination practice. Tanzania has different bacterial and viral illnesses and variable vaccination rates, despite country-wide efforts to ensure universal coverage of all children. *Haemophilus influenza* type b (Hib), while nearly eliminated as a serious bacterial infection in the United States after a comprehensive vaccination campaign in the 1990's, still remains a significant burden of disease in resource limited settings such as Tanzania. In 2009, Tanzania implemented Hib vaccine into their childhood immunization schedule and reported vaccinating 91% of their target population in 2010. As the Hib vaccine was not routinely offered prior to 2009, there are many children that are still susceptible to serious Hib-related infections (21). The WHO estimates that Hib is responsible for more than 3 million serious illnesses worldwide and approximately 386,000 deaths per year with a majority of the victims under 5 years of age (22) .

Malaria, a dangerous mosquito-borne parasite found throughout sub-Saharan Africa, also poses a significant threat to the pediatric population (14,23). The World Health Organization (WHO) estimates that in 2010 malaria was responsible for approximately 655,000 deaths(22). A vast majority of these victims were children and the WHO

estimates that one child dies every minute from malaria, accounting for approximately 22% of all childhood deaths. Oftentimes, these patients present to the EMD with prolonged fever, and malaria testing is imperative to management, as malaria is not treated by the antibiotics commonly given for other conditions.

The availability of diagnostic tests, however, is limited in health facilities in sub-Saharan Africa, especially tests for diagnosing bacterial illness(24), and acute care providers must often rely on clinical findings and results from incomplete diagnostic workup to manage febrile illnesses in children. Incomplete workup may contribute to increased morbidity and mortality, especially in the setting of malaria and bacterial co-infection. If a febrile child has a positive rapid malaria test, often no further tests are done to evaluate other possible causes of fever. Studies shows that concurrent bacterial infections in children with malaria is underestimated (24), and that up to 12% of children with severe malaria are also bacteremic(25).

The clinician must also consider the possibility of concurrent viral and bacterial infections in febrile pediatric patients presenting to the EMD. In a 2004 study of children under 60 days of age, Levine showed that even those with laboratory confirmation of respiratory syncytial virus, had a notable rate of concurrent bacterial urinary tract infections, suggesting that urine culture remains an important part of the diagnostic evaluation of young children even when another diagnosis is confirmed (26) .

The assessment of the patient's overall appearance is crucial and while there is an imperfect correlation between physical exam findings and bacterial illness, ill-appearing children are more likely than well-appearing children to have serious bacterial infections (27). Physical exam is a critical piece of the workup and management of children with

fever and may indeed reveal an obvious source of infection, thereby decreasing the need for additional testing and allowing for more appropriate treatment.

While there have been multiple attempts at devising clinical treatment guidelines and algorithms for pediatric patients presenting with fever, none of which fully address the diversity of potential infectious causes of fever in sub-Saharan countries like Tanzania. The MNH EMD was opened in 2010 and currently cares for an average of 120 patients per day, approximately 25% of who are children, and fever is a common presenting complaint (28).

2.0 PROBLEM STATEMENT

Resource-limited acute care settings present a special challenge for the management of febrile children less than five years old. There are no published stratifications specific for sub-Saharan Africa, where the etiologies of fever and patient vaccination status may differ substantially from other regions, making it difficult to predict the risk for serious infection. Beyond this, little is known about the actual clinical presentations, diagnostic management, and ultimate emergency provider clinical impressions of febrile children less than five years old presenting to acute care settings in the area. Currently, at MNH EMD, each physician uses individual clinical judgment for evaluating children under 5 years with fever, and it is unclear which tests physicians are utilizing in an attempt to diagnose and stratify these patients.

3.0 RATIONALE

Characterizing the current diagnostic management and emergency provider clinical impression of febrile children less than five years old presenting to the MNH EMD will serve as a basis for future development of management algorithms to improve early diagnosis and appropriate treatment. The ultimate goal is to provide prompt and effective care, while minimizing misdiagnosis and inappropriate use of antibiotics and anti- malarial medications.

4.0 OBJECTIVES OF THE STUDY

4.1 Broad objective

To describe the clinical presentations, diagnostic evaluation, treatment and emergency provider clinical impression of febrile children less than five years old at MNH EMD in Dar Es Salaam, Tanzania.

4.2 Specific objectives

1. To determine the specific type and frequency of laboratory and radiographic testing used in the evaluation of febrile children less than five years old.
2. To determine the immunization status of febrile children less than five years old presenting to the EMD
3. To determine the rate of abnormal physical findings in febrile children less than five years old presenting to EMD
4. To determine the rate of abnormal vital signs findings in febrile children less than five years old presenting to EMD
5. To determine top ten emergency provider clinical impressions of febrile children less than five years old presenting to the EMD

5.0 MATERIALS AND METHODS

5.1 Study Area

The study was conducted at the EMD of MNH, which is a tertiary referral hospital in Dar Es Salaam, Tanzania. The EMD receives patients from within Dar Es Salaam and the surrounding regional and district hospitals. The department receives 100- 150 patient per day, of which 25% are pediatric and many of which present with fever as a chief complaint.

5.2 Study Design

This was a descriptive observational study of pediatric patients presenting to the MNH EMD with a history of fever or documented fever.

5.3 Target Population

The target population is pediatric patients presenting to an African acute care setting with fever

5.4 Accessible Population

Pediatric patients presenting to the MNH EMD with fever.

5.5 Study Population

Inclusion criteria: all children less than 5 years old presenting to MNH EMD with documented or reported fever.

Exclusion criteria: patients presenting in cardiac arrest.

5.6 Data Collection Technique

We enrolled a convenience sample of children less than 5 years of age who presented with fever, defined as a axillary temperature of ≥ 37.5 degrees Celsius as rectal temperatures are not routinely performed in our department and rectal thermometers are not available. We excluded patients who presented in cardiac arrest. The parents of eligible children were approached and offered the opportunity to participate. Written informed consent was obtained from those who agreed. The treating physicians prospectively completed a standardized data collection form, including demographic data, vital signs, immunization history, pertinent data from the history and physical examination, laboratory results, treatment delivered, and emergency provider clinical impression .All diagnostic and treatment decisions were made at the sole discretion of the treating physician. For patients referred directly from another facility, we also recorded the referral diagnosis and treatment received prior to arrival.

5.7 Sampling Design

We enrolled a convenience sample of children less than five years old presenting to the EMD with documented or reported fever at times when research personnel were available for enrollment.

5.8 Recruitment and Informed Consent

Parents were informed of the study and offered the opportunity for their children to participate. The purpose of the study was explained to potential participants, and they were informed that participation was entirely voluntary and that their decision to participate or not would not impact their care. Children of parents providing informed

consent were enrolled in the study. Parents were also be informed of their right to terminate their child's participation in the study at any point in time.

5.9 ETHICAL CLEARANCE

Clearance was obtained from the MUHAS research committee and permission to conduct the study obtained from the respective department. Information from the patients was kept confidential. During and after the study, all data forms were kept in locked cabinets or on encrypted laptops and servers.

5.10 DATA ANALYSIS

Treating physicians prospectively completed a standardized data collection form, recording demographic data, vital signs, immunization history, pertinent data from the history and physical examination, laboratory results, treatment delivered, and EMD differential diagnosis and treating physician clinical impression. All diagnostic and treatment decisions were made at the discretion of the treating physician. For patients referred directly from another facility, we also recorded the referral diagnosis and treatment received prior to arrival. The study data were entered into an Excel database (Microsoft Corporation, Redmond, WA, USA).

Data was entered into Excel spread sheet and imported into statistical software (SAS Version 9.3). All data was cleaned and checked for any outliers or questionable entries using PROC (procedure), FREQ and UNIVARIATE. Cross-tabs were performed to check for "any" instance of condition within a series of variables to verify if present or not. (Study population, N=105). Patient descriptive characteristics are reported, including means, medians, and standard deviation.

6.0: RESULTS

6.1: Descriptive characteristics of the study population

We enrolled 105 febrile children less than five years old in the study. Mean age was 17.96 months (sd 14.83), and median age was 14 months, with a range from one month to 60 months. Eighty percent of children were above 6 months, and 64% were male. Sixty-four (61%) patients had fever at presentation (axillary temperature ≥37.5° C). 24 (22.9%) patients had fever documented at peripheral hospital and 17 (16.2%) only reported fever. Neonates were not enrolled in our study since they have separate neonatal unit. In the table below we stratify by age using categories commonly used in prior literature on febrile children presenting to emergency settings. (Table 1)

Table 6.1: Descriptive characteristics of the study population

Age	All (N=105)
Overall (median, range)	1-60 months, median 14 months
1 to 3 months	9 (8.6%)
3 to 6 months	12 (11.4%)
> 6 months	84 (80%)
Gender	
Female	38 (36.2%)
Male	67 (63.8%)

6.2: Patient history (treatment prior to arrival, birth history, medical history, immunization status

Since Muhimbili is a tertiary referral hospital, the majority of patients (54.3%) were referred from outside hospitals. Among children under 5 years referred from outside facilities, 71 (68%) received at least one dose of an antipyretic prior to arrival at MNH, 52 (50%) received antibiotics, and 32 (30%) received anti-malaria medications, Twenty-five (24%) received intravenous fluids and 4 (3.8%) received a blood transfusion. Among the overall cohort, 99 (94%) were born full term, while 10 (9.5%) had a history of birth complications, and 6 (5.7%) were born preterm (gestational age <37 weeks).

Nine patients (9%) had a history of any chronic illness, including congenital heart disease (3), sickle cell anemia (3), asthma (2), and HIV (1). All patients were vaccinated for polio (oral polio vaccine administered at birth), 100 (95%) for diphtheria-pertussis-tetanus toxin / Hepatitis B, 96 (91%) for BCG, 69 (66%) for measles, and 56 (53%) for Haemophilus influenza B. None of the children under 5 years were vaccinated for streptococcal pneumonia vaccine, since it was not included in national vaccination strategy at the time of the study (Table 2).

Table 6.2: Patient History

Fever at EMD	64 (61%)
Fever documented at peripheral hospital	24 (22.9%)
Fever reported by parents	17 (16.2%)
Referred	57 (54.3%)
Treatment prior to arrival	
Antibiotics	52 (49.5%)
Ant malarial	32 (30.5%)
Antipyretic	71 (67.6%)
IV fluids	25 (23.8)
Blood transfusion	4 (3.8%)
Birth history	
Term birth	99 (94.3%)
Preterm birth	6 (5.7%)
Birth complications	10 (9.5%)
Medical history	
Congenital heart disease	3 (2.9%)
Sickle cell anemia	3 (2.9%)
Asthma	2 (1.1%)
HIV/AIDS	1 (1.0%)

Immunizations	
DPT-Hb	100 (95.2%)
Polio	105 (100%)
Measles	69 (65.7%)
Haemophilus influenza	56 (53.3%)
Bacillus Calmette–Guérin	96 (91.4%)

6.3: Patients clinical presentations

The predominant symptoms from this cohort of febrile children less than 5 years old were poor feeding (47.6%), vomiting (42.9%), cough (34.3%), difficulty in breathing (28.6%), diarrhea (22.9%), abdominal distension (14.3%), and convulsion 14 (13.3%) (Table 3). Eighty-two (78%) had at least one vital sign abnormality at time of presentation, including fever 64 (61%), tachypnoea in 62 (59.1 %), tachycardia in 39 (37.1%), hypoxia in15 (14.3%) abnormal random blood sugar level in 31 (29.4%) and hypotension in 2 of 32 (6.25%) children under 5 years in whom blood pressure was measured. (Table 3).

On the physical examination of the patients, 86 (81.9%) had some abnormal physical examination finding at presentation. The most commonly affected systems were cardio-respiratory 74 (70.5%), neurological 29 (27.6%), abdomen 28 (26.7%), HEENT/ neck 22 (20.95%) and skin 12 (11.4%) (Table 3)

Table 6.3: Patient Clinical Presentation

Symptoms	**Present N=105**
Cough	36 (34.1%)
Dyspnea	30 (28.6%)
Cyanosis	1 (1.0%)
Altered mental status	11 (10.5%)
Seizure	14 (13.3%)
Rash	4 (3.8%)
Swelling	13 (12.4%)
Vomiting	45 (42.9%)
Diarrhea	24 (22.9%)
Abdominal distention	15 (14.3%)
Jaundice	13 (12.4%)
Decreased urine output	5 (4.8%)
Not passing stool	6 (5.7%)
Poor feeding	50 (47.6%)
Vital signs abnormalities	
Hypotension	2 (6.3%)*
Tachycardia (N)	39 (37.1%)
Tachypnoea(N)	62 (59.1%)
Fever at presentation(N)	64 (61%)

Hypoxia(N)	15 (14.3%)
Random blood glucose hypoglycemia (m mol/l) hyperglycemia(m mol/l)	31 (29.5%) 11 (10.5%) 20 (19%)
any abnormal vital	82 (78.1%)
Physical examination	Any abnormal findings
Neurological	29 (27.6%)
HEENT/Neck	22 (21%)
Cardio respiratory	74 (70.5%)
Abdomen	28 (26.7%)
Skin	12 (11.4%)
Any abnormal physical exam finding	86 (81.9%)

*blood pressure was recorded only in 32 patients due to lack of an appropriately sized cuff and 2 (6.3%) of these had hypotension for age.

6.4: Laboratory and radiographic evaluation

EMD diagnostic evaluation involved a number of point-of-care tests, laboratory investigations, and imaging studies. Point-of care tests included random blood glucose on all children (100%), malaria RDT on 103 (98.1%), urine dipstick on 30 (28.6%), rapid HIV testing on 26 (24.8%) and venous blood gas on 59 (56.2%). Among children under 5 years receiving these tests, 11 (10.5%) had an low blood glucose, 9 of 103 tested (8.7 %) were positive for malaria, 17 of 30 tested (56.7%) had a urine dipstick showing evidence of infection (leukocyte esterase or nitrite positive), and 5 of 26 tested

(19.2%) were positive for HIV. Laboratory investigations included blood smear for malaria in 102 (97.1%), complete blood count and chemistry panel in 100 (95.24%), venous blood gas analysis on 59 (56.2%), lumbar puncture in 6 (5.7%), blood culture in 6 (5.7%), urine culture in 11 (10.5%), and CSF culture in 2 (1.9%). Out of the children receiving these laboratory studies, 85 (100%) had an abnormal CBC, 46 (62.2%) had an abnormal chemistry, 6 (5.9%) were positive for malaria, 28 (52.5%) had an abnormal VBG, 1 (33.3%) abnormal lumbar puncture, 1 (16.7%) positive blood culture, 3 (33.3%) positive urine culture, and 1 (50%) positive CSF culture. Imaging studies included chest x-ray and plain abdominal x-ray, which were performed on 27(25.7%) and 4 (3.8%) patients, respectively. Out of the patients receiving imaging studies, 19 (70.4%) had an abnormal chest x-ray and 4 (100%) had an abnormal plain abdominal x-ray (Table 4).

Table 6.4: Laboratory and Radiographic Evaluation

Test	Number of children <5 years receiving the test (%)	Number of results available	Number of children <5 years with Abnormal results
Laboratory			
Rapid blood glucose (N=105)	105 (100%)	105 (100%)	11(10.5 %)
Rapid HIV	26 (24.8%)	26 (100%)	5 (19.2%)
Blood gas analysis	59 (56.2%)	53 (89.8%)	28 (52.5%)
Rapid malaria test	103 (98.1%)	103 (100%)	9 (8.7%)
Blood smear for malaria	102 (97.1%)	102 (100%)	6 (5.9%)
Full blood picture	100 (95.2%)	85 (85%)	85 (100%)
Chemistry panel	100 (95.2%)	74 (74%)	46 (62.2%)
Urinalysis(urine dipstick)	30 (28.6%)	30 (100%)	17 (56.7%)
Lumbar puncture	6 (5.7%)	3 (50%)	1 (33.3%)
Blood culture	6 (5.7%)	6 (100%)	1 (16.7%)
Urine culture	11(10.5%)	9 (81.8%)	3 (33.3%)
CSF culture	2 (1.9%)	1 (50%)	1 (50%)
Radiographic			
Chest x-ray	27 (25.7%)	27 (100%)	19 (70.4%)
Other radiographic test	4 (3.8%)	4 (100%)	4 (100%)

6.5: Treatment received in the emergency medical department

While in the EMD, most children under 5 years received at least one therapeutic treatment. Seventy-three (70%) of the febrile children under 5 years received at least one antibiotic, while only 13 (12%) received anti-malarial medications. Fifty seven (54%) received intravenous fluids and 43 (41%) received an anti pyretic (Table 5).

Table 6.5. Treatment received in the EMD

Treatment	**All (n=105)**
Antibiotics	73 (69.5%)
Anti-malarial	13 (12.4%)
Antipyretic	43 (41.0%)
Antibiotic and anti-malarial	6 (5.7%)
IV fluids	57 (54.3%)
Blood transfusion	2 (1.9%)
	105 (100%)

6.6: Disposition of febrile children to various wards

Eighty two percent of febrile children under 5 years were admitted to pediatric wards (general wards, malnutrition, diarrhea, burn unit and pediatric surgery), one child was taken directly to theatre due to bowel obstruction, 15 (14.3%) were discharged home and 2 (1.9%) died at the emergency department. Of the two children who died at the EMD, one died due to respiratory failure secondary to very severe pneumonia, and the second due to sepsis from intussusception with perforation. (Table 6).

Table 6.6: Disposition

Disposition	All (N=105)
General ward	87 (82.9%)
Home	15 (14.3%)
Theatre	1 (1.0%)
EMD death	2 (1.9%)
	105

6.7: The top ten emergency physician clinical impressions

The top ten emergency physician clinical impressions were malaria in 26 (24.3%), pneumonia in 16 (15.2%), septicemia in 10 (9.5%), urinary tract infections in 8 (7.6%), acute watery diarrhea with dehydration in 7 (6.7%), meningitis in 5 (4.8%), anemia in 5 (4.8%), skin and soft tissue infections in 5 (4.8%), bowel obstructions in 4 (3.8%), and pulmonary tuberculosis, sickle cell disease, and hepatitis accounted for 3 (2.9%) each.

Table 6.7 Top Emergency Provider Clinical Impressions in the EMD.

Provider Clinical Impressions	**Frequency**
Malaria	26 (24.3%)
Pneumonia	16 (15.2%)
Septicemia	10 (9.5%)
Urinary tract infection	8 (7.6%)
Acute watery diarrhea with dehydration	7 (6.7%)
Meningitis	5 (4.8%)
ANEMIA	5 (4.8%)
Skin and soft tissue infections	5 (4.8%)
Intestinal obstruction	4 (3.8%)
Pulmonary tuberculosis	3 (2.9%)
Sickle cell disease	3 (2.9%)
HEPATITIS	3 (2.9%)
Other	10 (9.5%)
	N=105

7.0 DISCUSSION

The purpose of this study was to describe the initial clinical presentation, diagnostic work-up, and emergency department management and emergency provider clinical impression of febrile children less than five years old presenting into an acute setting. This is the first study to describe and quantify the pediatric population seen in a tertiary emergency department in a sub-Saharan African country.

Our study enrolled a convenience sample of 105 febrile children less than five years old from August 2012 through November 2012. All patients enrolled had reported or documented fever and those with documented fever and fever at presentation a temperature of ≥37.5ºC axillary was considered as inclusion criteria. We also enrolled those children less than five years with reported fever by parents/caregivers because prior studies shows that the sensitivity of fever by touch is 89.2% (44). We enrolled only children less than five years old with fever because these age group is at greater risk of morbidity and mortality and immunization coverage is targeted in these age group, While only 62% of children had fever at the time of presentation 41% receive ant-pyretic at the emergency department, and significant proportion had received anti-pyretic prior to arrival. Prior studies have shown that antipyretics will not affect the cause of fever and sometimes makes difficult to diagnose (1).

We stratified by age using categories commonly used in prior literature on febrile children presenting to emergency settings (2,15). In some cases, these are derived from vaccination schedules that are similar but not identical to those used in our region. However, we felt that these categories would best allow comparison to existing literature.

Muhimbili is tertiary care hospital, and most patients seen there are transferred from district hospitals when they require a higher level of care. In our cohort, a significant proportion (46.7%) of children were self referrals. For comparison, one study from an emergency department in Netherlands found that most of the children presenting acutely were self referral (62%) , while 38% were referred by general practitioners from outside hospitals (29).

While there is no comparison data from the sub Saharan African region, the admission rate in our cohort was very high (85%) compared to published rates from other countries. Despite the fact that our population included a high number of self-referrals, and facility referral is the usual path to care at a tertiary facility like Muhimbili, the high admission rate suggests that many parents properly judged the severity of their child's illness and their need for emergent care(29). While other factors (diagnostic testing needs, long travel times) do contribute to admission decisions, the high rate suggests that the acuity of the population presenting to MNH EMD is high compared even to other limited-resource settings. In one comparative study from Malaysia, the pediatrics admission rate due to all causes was 25% (5), and the admission rates from the developed world were <10%

Vital signs help providers to identify children requiring immediate intervention. From this cohort of febrile children less than 5 years old, 78% had at least one vital sign abnormality at time of presentation, including fever (59.1%) tachypnea (59.1 %), tachycardia (51.4%), hypoxia (14.3%) , and hypotension (6.3%). The rate of abnormal random blood sugar (29.4%) was also very high, with 10.5% having hypoglycemia and

19% having hyperglycemia. Immediate interventions include airway protection, suctioning, oxygen administration, intravenous/intraosseous fluid boluses, ant-pyretic administration and correction of hypoglycemia.

The predominant symptoms from this cohort of febrile children less than 5 years old were poor feeding 50 (48%), vomiting in 45 (43%), cough in 36 (34%), difficulty in breathing in 30 (29%), diarrhea in 24 (23%), abdominal distension in 15 (14 %), and convulsions in 14 (13.33%). These results are similar to prior literature showing that respiratory symptoms and diarrhea are common symptoms in children visiting the ED overall (6), and that respiratory symptoms followed by gastrointestinal symptoms are the commonest symptoms associated with fever(29). Interestingly, though these symptoms are non-specific and may be associated with a range of conditions including many serious bacterial infections(30), emergency providers in our study still had the impression that febrile illness in children mostly is caused by malaria.

An appropriate diagnostic evaluation of febrile children in emergency department depends on age, history and physical examination findings. In order to identify the underlying cause of fever we need proper diagnostic tests that can rapidly identify a wide range of organisms including bacteria, virus, parasites and fungi. Our study suggests that some diagnostic tests may be underutilized in the EMD. For instance, urine dipstick which is a chemical tests for detection of leucocytes esterase or nitrites was performed in only 30 (28.6%) of the febrile children, but over half (57%) of the tests came back positive. This test is rapid and inexpensive it has sensitivity of 67%-85% for positive leucocytes esterase and specificity of 95%-99% for positive nitrites. Possible

causes of under utilization include difficulty with specimen collection, unavailability of supplies and lack of protocols (31). Studies show that the prevalence of UTI in children presenting to the ED with a fever may be as high as 8% (32). Even when children receive adequate empiric coverage with antibiotics, a missed diagnosis of UTI can result in delayed evaluation for structural problems leading to renal complications later in life. Emphasis should be on adequate diagnostic evaluation on those febrile children at risk for UTI. In addition, the proportion of abnormal chest x-rays was 70% of the 27 (25.7%) children in whom they were performed. While x-ray was performed in only a quarter of children, sixty-two (59%) of children had tachypnea, which is sensitive sign for pneumonia in febrile children(2). One study done in febrile infants found that 31% with any abnormal respiratory sign or symptoms had abnormal chest x ray(33). Increasing the utilization of imaging studies may help to rapidly identify or rule out a pulmonary source of infection and expedite disposition for all children with any respiratory symptoms or signs (34).

Malaria continues to be an ongoing public health concern in Tanzania, with an estimated prevalence of 13.6% during the rainy season and 3.3% in the dry season. This study was done in Dar Es Salaam (35) Often any febrile illness is considered to be malaria in children living in sub-Saharan Africa due lack of diagnostic tests to identify other sources. Currently the availability of rapid diagnostic tests for plasmodium falciparum, which provide results in 5- 20 minutes, have lessened the inappropriate use of anti malarial agents and improved diagnostic accuracy when compared to microscopy (36–38).

A systemic review found that under five mortality resulted predominantly from pneumonia 14%, diarrhea 9.9% and malaria 7.4% (39). In our study, rapid diagnostic testing for malaria was done for 103 (98.1%) febrile patients and was positive in 9 (8.7%), while anti-malarial were given in 13 (12.4%) of febrile children in the department. One study done in rural western Tanzania found that 12% of children had confirmed parasitological diagnosis for malaria(23). However, 30 patients in our study had received anti-malarial prior to arrival. Malaria was the top EMD clinical impression for 26 (25%) patients, and 13 (12%) children were treated for malaria at EMD while testing was positive in only 9 (8.7%) children overall. This discrepancy may be due to a combination of many patients receiving treatment prior to arrival at Muhimbili, test sensitivity, providers over-attributing fever to malaria, and poor documentation of management referring facilities. Some transferred patients may have been RDT positive at the district hospital, but negative after partial treatment. According to one study, 64% of patients remained RDT-positive on treatment day 2, while only 20% were positive after one week of therapy (40). The rapid malaria test used in our EMD, the SD Rapid Test™, has a reported 87% sensitivity and 99.5% specificity, according to manufacturer brochure. This test detects antibodies in the blood for plasmodium falciparum and plasmodium vivax.

In our study all children were checked for blood sugar level and approximately one-third had abnormal blood sugar level, including 10% with hypoglycemia which suggests that this is an essential test in febrile children. The complete blood count with differential was performed in 100 (95.2%) and results was available for 85 children less than five years old and all were abnormal. Anemia had contributed significantly to this finding

since current prevalance of anemia in Tanzania ranges from 59%-87% (15, 43) and our cohort was a hospital based which includes a group a very sick children. However, the delay in receiving white blood cell count results and sporadic availability of blood cultures continues to impede our ability to rapidly diagnose and treat infection. A systematic review and meta analysis was done in African countries about community acquired blood stream infections, and found that the prevalence of bacterial infection in febrile children <5 years is 18.3% and bacterial infection is associated with high morbidity and mortality(7). This suggests that diagnostic testing is an important adjunct to the physical exam. Our results show that, nearly two thirds of febrile children had abnormal electrolytes, and this could be as a result of history of diarrhea, vomiting and poor feeding. Identifying these children with electrolyte imbalance is key for successful management and a better prognosis. A recent study done in India, revealed that acute diarrhea is the second leading cause of death in children under five years and fluid and electrolytes replacement is the key stone for the management.(41)

Rapid HIV testing in our setting is usually done in those with a history and physical examination suggestive of HIV disease, and here was done in 26 (25%) of children. Of those tested (19.2%) tested positive. The high rate of seropositivity in this pediatric population is likely due to only testing patients with a history and exam highly suspicious for HIV/AIDS. The overall prevalence rate of HIV in Tanzania is estimated to be 5.8% in adults ages 15-49 and there are an estimated 240,000 children aged 0-14 living with HIV (21). In other countries, emergency departments have been an important site for early diagnosis of HIV via screening. However, we would require a more robust counseling and referral program to implement a screening program in our department.

Presentation was quite delayed, as the average time elapsed between presentation to a referral facility and arrival at MNH EMD for those children who were referred was 3.62 days (sd 4.12). Fifty-two (50%) received antibiotics prior to arrival and 73 (70%) received antibiotics in the EMD prior to disposition to the wards. Many children who were given antibiotics prior to arrival were also given repeat antibiotic at the emergency department either because time elapsed or because initial treatment not appropriate or specific agent was uncertain or child not improving on the given medications.

Twelve percent of febrile children less than five years old received anti-malarial in the EMD though only 9 (8.6%) had positive rapid malaria test which suggests that some children are treated for malaria despite negative rapid malaria test.

The top two emergency provider clinical impressions were malaria followed by pneumonia; however, based on EMD point of care results, only 9 (8.7%) children were diagnosed with malaria, while 19 (18%) were diagnosed with pneumonia by chest x ray. This suggests that pneumonia is a leading cause of admission in this cohort of febrile children and that emergency providers should have a higher degree of suspicion and a lower threshold for testing in children with respiratory findings. There is an overlap of symptoms between malaria and pneumonia(42), and in fact, many children with other primary clinical impressions had pneumonia listed as a second or third impression. Our results suggest that there is likely value to increased use of diagnostic testing that is currently available at the EMD.

8.0 LIMITATIONS OF THE STUDY

1) The results of these findings may not be the representative of the general population since the sample size was small

2) Lack of adequate diagnostic facilities and inability to collect optimal specimen types may impact the rate of diagnostic testing as well as the results, especially for cultures of urine, blood and CSF. The hospital-wide low rate of positive blood cultures in patients highly suspected of bacterial infection, for example, is often identified by providers as a reason why they do not often send blood cultures.

3) Incomplete laboratory results for some studies has led to analysis of the data which did not include some results requested by physicians. However, we doubt that this will result in systematic bias as it is unlikely to be correlated with illness characteristics.

5) The gold standard for fever definition is rectal temperature, which is not done in our setting; we may have failed to capture some febrile infants due to not measuring temperature rectally.

9.0 CONCLUSION

In MNH EMD, a range of diagnostic tests are used to determine cause of fever though testing results do not always correspond with reported clinical impressions. Malaria was listed as number one emergency provider clinical impression while only few febrile children less than five years old had malaria. Other diagnostics tests were underutilized, especially those for diagnosing bacterial infections. Many patients were diagnosed clinically with pneumonia without diagnostic imaging.

In referred patients, administration of antipyretics, antibiotics, and anti- malarial was common. Majority of febrile children less than five years receive antibiotic prior to arrival or at the ED , demonstrating that the majority of febrile children are treated empirically with antimicrobials with only limited diagnostic work up for the underlying cause of fever. Bacterial infections were very common among children who were tested.

10.0 RECOMMENDATIONS

1) We recommend the development of a symptom-based diagnostic testing protocol to rationalize our approach to diagnosis and management of febrile children less than five years

2) We recommend execution of larger prospective study with definitive testing to further characterize the etiology of febrile illnesses in acute care settings in this region.

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8.2 CONSENT FORM: (SWAHILI)

Fomu ya ridhaa katika utafiti wa "Tathmini juu ya dalili na vipimo vinavyotumika katika kuchunguza magonwa mbalimbali ya watoto chini ya umri wa miaka mitano yanayosababisha na joto kali la mwili hospitali ya taifa ,Muhimbili."

Utambulisho
Habari za saa hizi,
Jina langu ni Dr. Faith H Ringo nafanya kazi katika hospital ya Muhimbili na pia ni mtafiti katika utafiti wa "Tathmini juu ya dalili na vipimo vinavyotumika katika kuchunguza magonjwa mbalimbali ya watoto chini ya umri wa miaka mitano yanayosababisha na joto kali la mwili hospitali ya taifa ,Muhimbili." Sasa nitakupa maelezo ya kina kuhusu utafiti huu na kasha nitakuomba ridhaa yako ya kushiriki katika utafiti huu. Endapo utakuwa na maswali yoyote nitafurahi kukujibu.

Malengo ya utafiti.
Utafiti huu unafanyika kwa nia ya kuchunguza dalili na aina ya vipimo vinavyotumika katika uchunguzi wa watoto wenye joto kali la mwili pamoja na aina za magonjwa yanayosababisha joto kuwa juu katika idara hii mpya ya ajali na dharura muhimbili hosipitali.
Ushiriki unahusisha nini
Watakaokubali kushiriki tutawahoji maswali kadhaa, kisha kupimwa kwa taratibu zote za kidaktari na kupewa matibabu husika

Usiri
Jina lako litaonekana katika fomu moja tu kwa ajili ya kutengeneza namba yako ya utambulisho wa siri. Ni namba hii tu itakayotumika katika fomu za maabara na katika komputa mahali ambapo maelezo haya yote yatahifadhiwa. Taarifa zote utakazotupa ni siri na zitatumika tu kwa ajili ya utafiti huu na kuboresha huduma ya afya katika mazingira ya kazi na elimu ya utoaji wa huduma bora za matibabu ya mwili kuwa na joto kwa watoto walio chini ya umri wa miaka mitano kwa wafanyakazi wetu na wagonjwa na sio vinginevyo. Hakuna mtu mwingine zaidi ya wanaohusika wa utafiti huu ,atakayesoma/kupata maelezo yako.
Faida na Athari
Faida utakayopata katika utafiti huu ni kujua kama mtoto anapokuwa na homa ni vipimogani na magonjwa gani ya hatari anaweza kuwa nayo ambayo yatagundulika kwa kufanya uchunguzi wa kina kutokana na umri wa mtoto. Tunatarajia

tutakachojifunza katika utafiti huu utaboresha huduma ya afya katika maeneo/mazingira ya kazi.

Uhuru wa kushiriki na haki ya kujitoa
Ushiriki wako katika utafiti huu ni kwa hiari kabisa na pia unayo haki ya kujitoa katika utafiti huu wakati wowote ule utakapojisikia kufanya hivyo. Uamuzi wako wa kushiriki katika utafiti huu ama la, hautaadhiri hata kidogo haki yako kama mgojwa ya kupata huduma na tiba.

Nani wa kuwasiliana naye.
Iwapo utakuwa na swali lolote kuhusu utafiti huu , unaweza kuwasiliana na
Dr Faith H Ringo; Chuo kikuu Cha Afya na Sayansi za tiba Muhimbili; Idara ya tiba; S.L.P 65001 Dar es Salaam. Simu 0715942246

AU
Professa M.Aboud Msimamizi wa utafiti huu :Chuo kikuu Cha Afya na Sayansi za tiba Muhimbili; S.L.P 65001 Dar es Salaam

Mimi _____
Nimeelewa maelezo yaliyoandikwa hapo juu na kuridihika na majibu niliyopewa kwa maswali yangu yote. Ninakubali kushiriki katika utafiti huu.
Jina la mshiriki: _____
Sahihi ya mshiriki: _____
Sahihi ya Shahidi: (kama mshiriki hawezi kusoma): _____
Tarehe ya kusaini ridhaa: _____

Pt initials:

FEBRILE CHILD STUDY

ANY QUESTIONS CALL: UPENDO GEORGE 0784 684 333, FAITH RINGO 0715 942 246

INCLUDE ANY CHILD WHO:

- ☐ Age ≤5years
- ☐ T ≥ 37.5C **or** T ≤35C during stay at EMD **or** Reported fever with THIS illness
- ☐ Not in cardiac arrest on arrival

PERSONAL INFORMATION

Name:	**Medical record number:**
Age (months/years):	**Date seen:**
Sex (M or F):	**Time arrived @ EMD:**
Address:	**Time seen:**
Phone no. 1:	**By Dr. :**
Phone no. 2:	**Responsible person:**

INFORMATION FROM REFERRING HOSPITAL

Referred from another facility? **Circle: Y or N. If NO, skip this box.**
Referral hospital: Number of days of admission **or** Admission date:
Referral diagnosis (list all):
List any prior facilities patient visited during this illness?
Treatment received prior to arrival at EMD **(mark Y, N or unk**), **if YES, name them**: - Antibiotics:

- Anti-malarial: - Anti-pyretic: - Other medications: - IV fluids prior to arrival at MNH -> Type: Amount:

HISTORY OF PRESENT ILLNESS

CHIEF COMPLAINT		
____mo/yo M/F w/ _____ for ___ days w/ associated: **[ ] cough x ____ days** **[ ] fever x ____ days** **[ ] AMS x ____ days** **[ ] Poor feeding x ____ days** **[ ] Other:**		
ROS (check all that apply)		
[ ] cough **[ ] dyspnea/SOB** **[ ] cyanosis** **[ ] other (list):**	**[ ] AMS** **[ ] seizures/convulsions** **[ ] fever** **[ ] rash** **[ ] swelling?**	**[ ] vomiting** **[ ] diarrhea** **[ ] abdominal distension** **[ ] jaundice** **[ ] decreased urine output** **[ ] not passing stool** **[ ] poor feeding**
PMH		
[ ] Term [ ] Preterm [ ] Unk **Complications with birth (describe):** **Chronic/congenital disease (check):** **[ ] Congenital heart disease [ ] Sickle cell anemia [ ] Asthma [ ] HIV/AIDS** **[ ] Other (list all):**		
Last antibiotic use (date):		
Hospitalization history (date and dx): **Surgical history (date and operation):**		
Immunizations per [ ] parent/guardian OR [ ] HPI card (check all that apply)		
[ ] DPT-Hb **[ ] Polio (OPV)** **[ ] Measles**		

[ ] Hemophilus
[ ] Others (list):

Current home medications (list all)

Prescription by doctor:

Bought at pharmacy w/o prescription:

Local herbs:

PHYSICAL EXAM

Triage VS: BP HR T (axillary/rectal) RR Sp02 % (RA/ __L NC/ __L NRB)

Resus VS: BP HR T (axillary/rectal) RR Sp02 % (RA/ __L NC/ __L NRB)

HEENT:
[ ] Bulging fontanelle [ ] Other:
[ ] Sunken eyes
[ ] Ear discharge / hyperaemic tympanic membrane
[ ] Stiff neck
[ ] Hyperaemic oropharynx

Neurology:
- Mental status: [ ] Alert [ ] Drowsy [ ] Irritable [ ] Stupor [ ] Coma
- Tone: [ ] Decreased [ ] Flaccid [ ] Hypreactive [ ] Hypertonia
[ ] Other:

Chest: [ ] RRR [ ] no murmur/rub/gallop Abnormal: [ ] tachycardic [ ] other:
[ ] NL effort, CTAB, no wheezes/rales/rhonchi Abnormal: [ ] wheezes, R/L
[ ] rales, R/L
[ ] rhonchi, R/L
[ ] increased WOB/retracting
[ ] tachypnea
[ ] other:

Abdomen:
Distended
Bowel sounds: absent/ reduced/ increased
Palpable organs/ masses.....

Skin / soft tissue
Rash.....

Cellulitis.....
Abscess.....

DIFFERENTIAL DIAGNOSIS (List):

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INVESTIGATIONS

X-ray /CT-scan: done at EMD / prior to arrival
Findings:

Laboratory results
RBG.....
RDT.....
Rapid HIV test.....
B/S for mps.....
CBC; WBC..... N .....M..... B..... E .....Bands.....
Hb..... Hct..... Platelets.....
Chemistry: Na..... K..... Cl..... BUN..... Cr .....Glucose..... Ca..... Lactate.....
ABG/VBG: pH ..... pCO2..... pO2 .....HCO3 .....An Gap.....
UA.....
CSF: clear / traumatic / purulent

Micro:
Cultures: urine / blood / CSF

TREATMENT

MEDICATION	DOSE	ROUTE	TIME GIVEN
IVF	AMOUNT	TIME	NOTES
BLOOD PRODUCTS	AMOUNT	TIME	NOTES

OTHER INTERVENTIONS (Intubation, procedures, etc)

Repeat VS						
Time	BP	PR	RR	Sp02	Temp	RBG

DISPOSITION

[ ] WARD A [ ] WARD B [ ] MAKUTI A [ ] MAKUTI B [ ] MORGUE
Time the patient leave EMD
Is the patient alive at disposition YES / NO If NO: Date of death Cause of Death
Is the patient alive at hospital discharge: YES /NO If YES: Date of discharge Discharge diagnosis If NO: Date of death Cause of death

FOLLOW UP AFTER DISCHARGE (at 14 days)

Date
Person reached / relationship to the patient
Is patient alive YES / NO If NO: Date of death
If alive, has patient returned to baseline activities/ school? YES/ NO If NO, explain
Has patient has unscheduled hospital / doctor visit since discharge? YES/ NO If YES, explain