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Triage guideline for immunocompromised children with fever in an emergency centre in Ethiopia

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ABSTRACT

Fever in children with neutropenia often portends life-threatening bacteremia that may be ameliorated with early recognition and the rapid administration of antimicrobial therapy. Studies demonstrating this effect have been done in resource-endowed countries, but not in resource-limited settings. We attempted to decrease the time to antibiotics in patients with fever and neutropenia presenting to a paediatric emergency centre at a tertiary care referral hospital in Ethiopia. In 3 phases we performed baseline data collection, instituted triaging and treatment guidelines, and provided antibiotics. We tracked a variety of outcomes, most importantly time from arrival to initiation of antibiotics. While this time was reduced during the guideline institution phase of our intervention, time reductions were inconsistent and not sustained. This was likely due to competing clinical priorities among providers caring for a high volume of ill children. While in the U.S., fever and neutropenia is easy to prioritise within the paediatric emergency centre, future quality improvement measures in this setting may have a greater benefit on critical presentations such as shock or respiratory failure. Alternative strategies geared towards general efficiency improvement and teamwork, rather than focusing on one patient group may be a higher yield approach for improving care in this paediatric emergency centre.

African relevance

- The study hospital is in East Africa and should have similarities with similarly resourced African hospitals.
- While fever and neutropenia are not necessarily the priorities, guideline-development for improved triage is a generalisable initiative for provision of care in similarly resourced settings.
- The limitation of competing priorities within a high acuity Paediatric Emergency Centre is relevant throughout the continent requiring these priorities to be balanced.

Introduction

Fever in children with neutropenia often portends life-threatening bacteremia that may be ameliorated with early recognition and the rapid administration of antimicrobial therapy. Studies in resource-endowed countries including the United States have demonstrated that delay in antimicrobial administration by 30 min can lead to an increase in mortality [1], and increased lengths of hospital stay [2]. Guidelines that streamline processes in the Emergency Centre demonstrate effectiveness at reducing the time to antimicrobial administration [3,4]. A standardised approach to rapid triaging with vital sign assessment, including assessment of known or suspected underlying immunocompromised patients, standardised diagnostics, and availability of empiric antimicrobial therapy tailored to local bacterial susceptibility patterns and common pathogens along with administration order sets and dedicated personnel, reduces delays in providing lifesaving care to critically ill patients in developed resource-endowed countries. Some guidelines attempt to risk stratify patients as high or low risk oncology patients with fever and neutropenia, even at times allowing for outpatient treatment, but they require patients to be well-appearing, have certain lab criteria, and have daily follow up and ability to easily get their antibiotic prescriptions [5,6].

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is a tertiary referral hospital that serves as the primary training site for the School of Medicine and College of Health Sciences. The capacity of the Paediatric Emergency Centre (PEC) is about 40 beds, with additional patients placed in chairs, and most patients housed in a single large room. The annual census is approximately 15,000 patients with lengths of stay in the PEC ranging from hours to weeks until discharge or admission to an inpatient ward. Patient care is provided by nurses and residents, with consultants overseeing their practice. Clinicians manage children with a range of paediatric cancer manifestations, all of whom are triaged through the PEC prior to admission to the 26-bed oncology unit, when census permits. The oncology ward is almost always full and priority goes to children requiring chemotherapy, so patients with fever and neutropenia must come through the PEC and many stay in the PEC for their course of treatment. Most medications must be purchased by family, collected from the pharmacy, and then given to the patient. At the time of our study, Black Lion was the primary referral center for all paediatric oncology patients in the country of Ethiopia, a country with a population of almost 100 million people. The average patient seen in the PEC at Black Lion is complicated and very ill, so prioritisation is difficult, and nurses typically cannot perform interventions without orders from physicians.

Studies of standardised approaches to management in PECs in resource- challenged countries are lacking. In contrast to settings where risk-stratification of patients based on timely laboratory results and universal availability of interventions are available, resource-limited settings may not have access to real-time laboratory diagnostics and interventions. Dependency on individual family financial resources and their time to procure diagnostic and intervention supplies challenges timely access to both.

The objective of this initiative was to improve the time to receipt of therapy in febrile children with known or suspected immunocompromising conditions. We hypothesised that implementation of standardised guidelines in PEC triage and in the treatment area would improve delivery of care, while providing resources to overcome accessibility barriers would optimise time to administration of antibiotics and other aspects of care.

Methods

We conducted a prospective study to standardise assessment and treatment initiation of children with known or suspected neutropenia and fever who presented for evaluation at the PEC at TASH from 17 February 2016 to 30 November 2016. No electronic records were being kept at the time to inform how many total patients were seen in the PEC during this time, but based on average numbers, it is likely about 15000.

A needs assessment conducted as part of an ongoing collaboration between Emory and Addis Ababa Universities demonstrated that process improvement in the PEC, focusing on children with fever and neutropenia, with the development of standardised guidelines in the PEC was a priority. We adapted existing triage/care guidelines used in resource-endowed settings to use in the TASH PEC to care for paediatric patients with fever and known or suspected neutropenia.

The three phases of the process improvement project were instituted based on an initial needs assessment and discussion with collaborators. We identified both the paucity of equipment to triage patients and an absence of documentation of timelines of interventions as two areas that were deserving of focus. The hypothesis was that increasing the documentation of timing of interventions would allow assessment of current status and measurement of change, and that standardising the triage process and subsequent steps of care would decrease the time it would take to provide antibiotics to this at risk population.

1) During the first phase (baseline) from 17 February 2016 to 9 April 2016, we provided wall clocks, thermometers, blood pressure cuffs and other basic equipment to facilitate triage. We trained clinicians to record demographic information (excluding personal identifiers), time of assessment and interventions including vital signs as components of the baseline data collection.
2) 2) During the second phase (implementation) from 10 April 2016 to 21 September 2016, we continued reminders about the documentation of demographics and timelines of interventions. We introduced standard guidelines for PEC triage adapted to TASH to clinicians in the TASH PEC by placing printed materials available in English and Amharic (Appendix A) in care areas where they were visible to staff as a reminder to follow each step in the provision of standardised patient care. We met multiple times with the nursing staff and medical house staff to review and explain the guidelines and to answer questions.
3) During the third phase (provision of blood culture bottles and antimicrobials) from 22 September 2016 to 30 November 2016, blood culture bottles were provided to the PEC through an unrelated funding mechanism. Empiric antibiotics were purchased by our project initiative from the pharmacy and were housed in a refrigerator in the PEC for use in children in conjunction with the guidelines. We also provided further reminders and education about guideline implementation to the PEC clinical staff. The plan was that if provision of antibiotics was helpful, the hospital would be willing to house a couple of doses of ceftriaxone and gentamicin in the PEC for quick use, that would then be refilled by the patient's families in the same way they typically pay for medications (Table 1).

Data collection in each of the three phases included the following variables: Demographic information (without personal identifiers) and clinical presentation, time from triage to vital sign measurement, physician evaluation, blood collection, fluid administration, and time of antibiotic administration. Standardised data collection forms, developed for the purpose of the study were used to collect data. Nurses received a nominal payment for each data collection form they completed.

Descriptive statistics were calculated for demographic and other variables of interest, including counts, percentages, means and standard deviations and medians and interquartile ranges. To examine overall differences among phases, a non-parametric, Kruskal-Wallis test, was used to calculate overall *p*-values. Multiple comparisons were performed to examine differences and calculate pairwise p-values between phases. Statistical significance was assessed at the 0.05 level unless otherwise noted.

Interrupted time series analyses (ITS) were used to assess changes in levels and trends before and after each intervention. To determine the effect of each intervention, significant differences between intercepts and slopeswere evaluated. Statistical analyses were performed using SAS 9.4 (Cary, NC). Graphs were generated, both including and excluding outliers, for time to vital sign assessment, time to physician evaluation, time to bloodwork, time to fluid administration, and time to antibiotic administration.

The protocol was reviewed by the Addis Ababa University College of Health Sciences and the Emory University Institutional Research

Table 1
Summary of phases.

Phase	Dates	Intervention
1	2/17/16–4/9/16	1. Provided clocks/healthcare equipment 2. Baseline data collection
2	4/10/16–9/21/16	1. Provided training to nurses and housestaff about fever and neutropenia 2. Instituted guidelines
3	9/22/16–11/30/16	1. Ongoing training 2. Ongoing guideline implementation 3. Provision of antibiotics and blood culture vials in the PEC

Table 2
(Baseline characteristics).

	Phase 1		Phase 2		Phase 3		p-value
	n	%	n	%	n	%	
Overall	36	30.0	67	55.8	17	14.2	
Status							0.45
Dead	3	8.3	6	9.0	0	0.0	
Alive	33	91.7	61	91.0	17	100.0	
Sex							0.70
Male	23	63.9	18	26.9	11	64.7	
Female	13	36.1	45	67.2	6	35.3	
Vitals (median [IQR])							
Temperature	34	38.6 [38.4–38.8]	66	38.6 [38.4–39.0]	17	38.6 [38.4–38.9]	0.32
HR	36	131 [118–150]	65	130 [118–150]	17	140 [128–149]	0.72
RR	33	30 [28–36]	46	30 [25–36]	17	28 [24–32]	0.43
SBP	26	97.5 [88–100]	39	100 [90–107]	9	90 [90–99]	0.29
DBP	26	60 [50–70]	39	60 [60–70]	9	60 [60–65]	0.71
SPO2	35	94 [92–98]	67	93 [91–95]	17	92 [91–95]	0.15

IQR: interquartile range, HR: heart rate, RR: respiratory rate, SBP: systolic blood pressure, DBP: diastolic blood pressure, SPO2: oxygen saturation.

Boards, who deemed that the study met necessary guidelines and was exempt from further review.

Results

Information from 120 unique subjects was collected during the 9 month study period; 36(30%) during phase 1; 67(56%) during phase 2; 17(14%) during phase 3. Demographic and baseline clinical data did not differ with statistical significance among the subjects included in each phase, (Table 2). Median time to antibiotic administration was statistically shorter in phase 3 compared to phases 1 and 2. Median time to vital sign recording was significantly shorter in Phase 3 compared to Phase1 (Table 3).

Time interval plots, created both including and excluding outliers, showed a decrease in the time from patient presentation in the PEC to antibiotic administration over the course of the Phase 1 and Phase 2 interventions, despite the length of Phase 2 being longer than Phase 1. There was a significantly longer initial time to antibiotic administration in Phase 2 compared to Phase 1 (p: 0.003) followed by a subsequent decrease during Phase 2. The time to antibiotic administration in Phase 3 was consistently short and remained fairly constant with a slight uptick towards the end of phase 3. (Fig. 1).

Additional time interval plots included time to secondary outcomes. Time to vital sign recording remained short throughout all phases though an increase during Phase 1 was evident. Time to vital sign recording from time of presentation in phase 3 remained constant. Time to physician evaluation did not show significant change in any phase. Time to phlebotomy generally increased as the phases progressed, though were significantly shorter at the beginning of Phase 3 (p: 0.02). A decrease in time to fluid administration in Phase 1 was shown. The time to fluid administration was significantlyshorter at the beginning of Phase 3 (p: 0.035). The trend (p:0.001) of the intervention in Phase 3 was also statistically significant, but showed that the time to fluid administration increased in Phase 3. There were a number of patients who did not receive fluids, however, which can affect the ability to interpret the results in regards to time to fluids (Fig. 1).

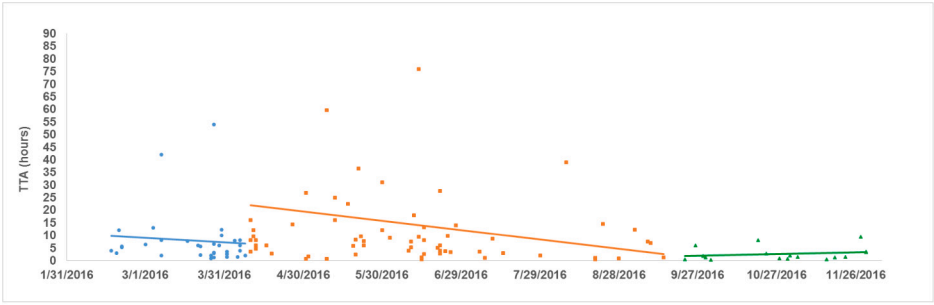
Discussion

During an 8-month study period consisting of three phases, a

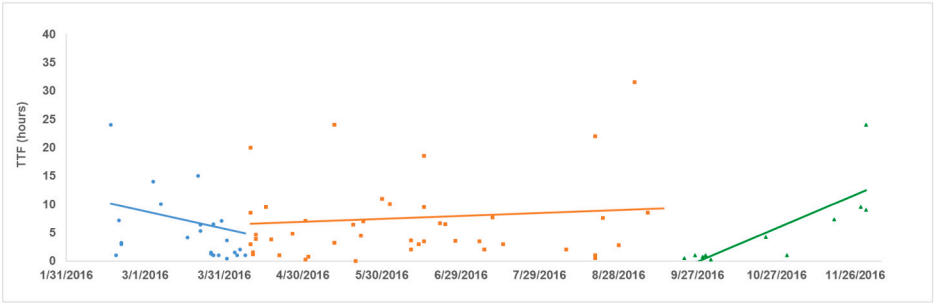
Table 3
Results.

Outcome	Phase 1	Phase 2	Phase 3	Overall *p* value	Pairwise p value		
					1 vs 2	1 vs 3	2 vs 3
TTA(hours)							
N	33	66	17				
Mean +/− SD	7.8 ± 11	14.6 +/− 25.1	2.7 +/− 2.7	0.055	0.255	0.659	0.075
Median (25th–75th)	5.6(2.5–7.8)	7.5(3.0–14.0)	1.5(0.8–3.3)	< 0.001	0.2950	0.004	< 0.001
TTV(hours)							
N	36	67	17				
Mean +/− SD	0.22 +/− 0.36	0.48 +/− 2.81	0.08 +/− 0.06	0.719	0.828	0.970	0.765
Median (25th–75th)	0.17(0.08–0.17)	0.08(0.05–0.17)	0.08 (0.08–0.08)	0.048	0.176	0.045	0.532
TTP(hours)							
N	36	67	17				
Mean +/− SD	0.91 +/− 1.88	0.60 +/− 0.59	1.15 +/− 3.19	0.635	0.864	0.425	0.385
Median (25th–75th)	0.50(0.25–0.92)	0.50(0.33–0.58)	0.41(0.30–0.50)	0.347	0.997	0.551	0.274
TTB(hours)							
N	36	61	17				
Mean +/− SD	2.91 ± 3.55	8.29 +/− 11.80	5.25 +/− 10.77	0.034	0.027	0.697	0.496
Median (25th–75th)	1.67(0.81–3.21)	2.33(1.00–10.67)	1.00(0.58–3.16)	0.055	0.149	0.630	0.137
TTF(hours)							
N	25	43	11				
Mean +/− SD	6.97 ± 10.93	7.71 +/− 9.13	5.33 +/− 7.14	0.755	0.948	0.882	0.739
Median (25th–75th)	3.25(1.00–7.08)	4.50(2.80–8.50)	1.00(0.80–9.00)	0.250	0.455	0.662	0.371

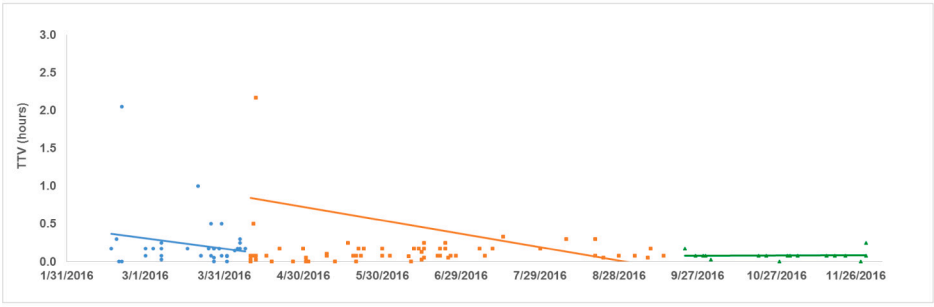
TTA: time to antibiotics, TTV: time to vitals, TTP: time to physician, TTB: time to blood draw, TTF: time to fluids.



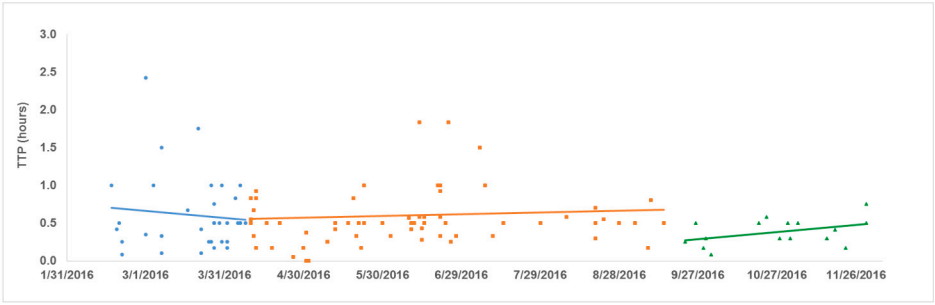
Time to Antibiotic Administration



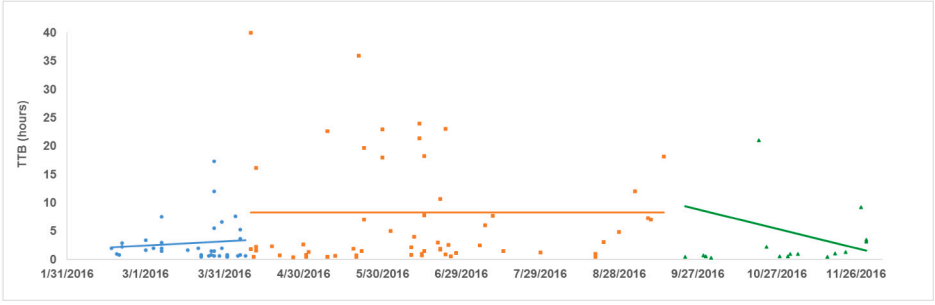
Time to Fluid Administration



Time to Vital Sign Recording



Time to Physician Assessment



Time to Blood Draws

Fig. 1. Time plots of data.

baseline phase, a guideline implementation phase, and provision of blood culture bottles and antimicrobials phase, we demonstrated variable impact of education, guideline implementation, and resource provision in a tertiary care paediatric emergency centre in Addis Ababa, Ethiopia. While phase 3 of our project demonstrated shorter overall time to antibiotic administration, only phase 2 (guideline implementation) demonstrated a significant decline in time to antimicrobial administration that was maintained during the phase. This decline in slope was not sustained beyond the phase 2 time period; administration times at the beginning of this phase were longer than in the pre-intervention phase. It is unclear why administration times were much longer at the beginning of this phase but this was the point at which we began providing extensive education to nursing staff and residents regarding the emergent nature of treating fever and neutropenia, and turn-over of doctors practicing in the PEC could contribute to the increase in time to intervention. The subsequent decrease in Phase 2 suggests a "learning curve" or initial time needed for the staff to learn and implement the intervention effectively. Additionally, regarding secondary outcomes, the shorter initial time to vital signs recording in Phase 2 compared to Phase 1 demonstrated an intervention effect (p: 0.04). The shorter time to phlebotomy at the beginning of Phase 3 also possibly represents an effect of the intervention during Phase 2. Lastly, the overall median time to antibiotic during phase 3 was both clinically and statistically significantly shorter than the median times in phases 1 and 2, suggesting an overall improvement in our primary outcome over the course of the trial. (Table 3 and Fig. 1) We were unable to analyse degree of illness in patients as a factor leading to timeliness of interventions and do not have seasonality data on likelihood of illness or volume of new admissions based on season, but as a referral center, the PEC remains busy with critically ill children year-round.

Despite collaboration with physician leaders and nursing management in the paediatric emergency centre, provision of resources and financial reimbursement to the study team, data collection activities and strict guideline adherence were inconsistent during phases 2 and 3. This might be due to competing clinical priorities such as a high volume of acutely ill patients with other medical problems. The re-education of rotating staff regarding data collection and study activities was an additional challenge. We were able to demonstrate that during the study period, the PEC mortality rate for the study-included patients remained low, but we have limited follow up data for patients after discharge from the PEC either to home or to the wards.

Conclusions

Our study demonstrated some of the challenges inherent in implementing and assessing guidelines in this resource-challenged setting. Firstly, while guidelines and nurse-initiated protocols are common in PECs in the United States, they are nonexistent in this PEC, making their acceptance even more difficult. Secondly, as this PEC cares for large numbers of critically ill patients, attention to the proposed interventions in these relatively less acute immunocompromised febrile children may have been deferred out of necessity. Even when providing the resources, which were perceived as barriers to care, such as laboratory supplies and antimicrobials, the phased interventions did not result in the sustained impact that was anticipated. In this setting, nurses are not able to provide medications without a physician order and the physicians working in the PEC change frequently. As the oncology ward is constantly at capacity with patients receiving chemotherapy, assistance from the oncology ward, or direct admission to the oncology ward for patients with acute concerns is not possible, and the ward is not able to easily deal with acutely ill septic patients. Despite ongoing and fruitful partnerships, the competing priorities of clinical care appeared to prevent optimal assessment of the interventions provided in the various phases. Task shifting, training, and creating roles for staff with less training than physicians or nurses, such as phlebotomists, or techs, may be an alternative cost saving method to improve efficiency in this environment, as relates to improving time to critical interventions such as antimicrobial administration. While development of guidelines could play a role in increasing care efficiency in this environment, their successful implementation likely requires a steady presence of people able to prioritise said intervention until its implementation is part of the normal flow of the PEC. This may be more successfully accomplished by concentrating on interventions that address general PEC efficiency rather than that specific to one patient population.

Dissemination of results

Results have been shared and discussed with the local participating physicians who have been involved in writing this paper and examining ways to move forward with various interventions in the PEC in Ethiopia. The paper itself, now formalised will be shared with permanent staff members in the hosting site.

CRediT authorship contribution statement

Authors contributed as follow to the conception or design of the work; the acquisition, analysis, or interpretation of data for the work; and drafting the work or revising it critically for important intellectual content: WA, TB, AS and TB contributed 25% each. All authors approved the version to be published and agreed to be accountable for all aspects of the work.

Declaration of competing interest

The authors declared no cinflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.afjem.2020.10.004.

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