Clinical Outcomes Before and After Implementation of a Pediatric Sepsis Protocol in a Resource-Limited Setting

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** Abstract

Introduction

Background: Sepsis shock has a high mortality rate in children in resource-limited settings and treatment is frequently complicated by malnutrition. Current guidelines recommend patients receive multiple fluid boluses, but excessive fluid is associated with significant morbidity and mortality. At the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) the mortality rate is ~60% in severely malnourished children with sepsis. Critically, in 2010, they implemented a pediatric sepsis protocol to improve the diagnosis and treatment of sepsis.

Objectives: Demonstrate that a pediatric sepsis protocol in this resource-limited setting can improve morbidity and mortality. Demonstrate that the duration and severity of malnutrition are independent risk factors for poor outcomes.

Methods: A retrospective cohort study of children 1-59 months with a diagnosis of sepsis, severe sepsis or septic shock admitted to icddr,b from 1/20/2009-10/25/2011. The primary outcome is mortality rate pre and post-protocol implementation. Secondary outcomes include fluid overload, heart failure, need for respiratory support, length of ICU stay, and length of hospital stay. Data analysis includes a logistic regression model and Fisher’s Exact Test. Clinical outcomes and mortality were stratified by degree of malnutrition. Protocol compliance was assessed by antibiotic administration within one hour of diagnosis.

Results: There were 325 patients included in the analysis: 143 before and 185 after protocol implementation. Pre- and post-protocol mortality and antibiotic administration within one hour of admission were lower and not statistically significant (32.1% vs. 34.99%, p=0.72; 18.05% vs. 12.54%, p=0.42, respectively).

Conclusions: Implementation of a pediatric sepsis protocol did not improve survival during the study period. Similar rates of early antibiotic administration suggest that there is poor protocol compliance. Though evidence-based treatment protocols are a potential cost-effective strategy to improve outcomes, the effectiveness of a sepsis protocol has yet to be demonstrated in the developing world. Future studies should focus on optimal implementation of a sepsis protocol in resource-limited settings.

** Introduction

Sepsis is a high mortality rate in children under 5 in resource-limited settings — 10-50% compared to 2-5% in developed countries [1]. Severe sepsis and septic shock: 2008. The pediatric sepsis protocol: • did not improve mortality • May have increased fluid overload, heart failure, need for respiratory support, length of stay and hospital stay • Protocol compliance: Antibiotic administration within 1 hour of admission • Pre-1:1.1% (151/13552); Post-1.0% (163/16362) • Increased rates of blood transfusions but not antibiotic administration • Risk factors for mortality include: • Acute on chronic malnutrition • Lower weight-for-age-Z-score • Lower hematocrit • Meeting severe sepsis criteria • Risk factors for fluid overload include: • Post-protocol implementation • Lower hematocrit • Receiving a blood transfusion

** Study Question

Can an evidenced-based pediatric sepsis protocol improve outcomes in a resource-limited setting?

** Hypothesis

A pediatric sepsis protocol improves outcomes and mortality rates in children regardless of nutritional status

• A pediatric sepsis protocol improves outcomes and mortality rates in children regardless of nutritional status

• Severely malnourished children have more fluid overload, heart failure and higher mortality

** Background

The International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) conducts research and delivers care to the country’s poorest residents. At icddr,b, pediatric mortality due to sepsis is 30% and 60% in severely malnourished children [2]. Severely malnourished children frequently develop heart failure and have high rates of complications and death [3].

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** Figure 1: The icddr,b Pediatric Sepsis Protocol Implemented in 2010 Based on the Surviving Sepsis Campaign (01)

** Results

** Study Design and Methods

Site: icddr,b (Dhaka Hospital); Bangladesh

Population: Children <5 years with and without malnutrition

Study design: Retrospective cohort study

Inclusion criteria: Age 1-59 mos, with a diagnosis of sepsis, severe sepsis or septic shock admitted to icddr,b 10/25/2009-10/25/2011. Identified cases and controls with a keyword search (“sepsis”, “septic”) of the electronic medical record. All others were excluded

Primary Outcome: Mortality rate pre- and post-protocol implementation

Secondary Outcome: Change in clinical outcomes (fluid overload, heart failure, need for respiratory support, length of stay and hospital stay).

Protocol compliance: Antibiotic administration within 1 hour of admission

Using R 3.0.1, the following tests were run: t-test (means), chi-square test (proportions), a logistic regression analyses. A probability ≤0.05 is considered statistically significant.

** Definitions

Wasting: weight-for-height reflects acute malnutrition

Stunting: height-for-age reflects cumulative effect of chronic malnutrition

Undernutrition: weight-for-age (WAZ) is a composite of wasting and stunting and does not distinguish acute from chronic malnutrition

Sepsis: infection AND >2 abnormalities in: temperature, heart rate, respiratory rate, white blood cell count, mental status

Severe sepsis: sepsis AND CV dysfunction OR ARDS OR >2 organ dysfunction

Septic shock: severe sepsis AND CV dysfunction despite 40ml/kg of fluid overload.

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** Table 1: Baseline Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pre-Protocol (N=57)</th>
<th>Post-Protocol (N=103)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality Rate</td>
<td>50% (28/57)</td>
<td>40% (41/103)</td>
</tr>
<tr>
<td>Median Age (in SD)</td>
<td>60.32 (18.65)</td>
<td>63.86 (18.65)</td>
</tr>
<tr>
<td>Median Predicted Probability of Death Based on 28-day mortality</td>
<td>0.64 (0.16)</td>
<td>0.64 (0.16)</td>
</tr>
<tr>
<td>Need for Respiratory Support, N (%)</td>
<td>49 (85.1)</td>
<td>39 (37.4)</td>
</tr>
<tr>
<td>Need for Cardiac Support, N (%)</td>
<td>28 (49.1)</td>
<td>20 (19.4)</td>
</tr>
<tr>
<td>Hematocrit, Mean %</td>
<td>36.03</td>
<td>31.59</td>
</tr>
<tr>
<td>Blood Saturation (SpO2), Mean (%)</td>
<td>90 (18.0)</td>
<td>90 (18.0)</td>
</tr>
<tr>
<td>Nutritional Status (WAZ)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal Status (WAZ)</td>
<td>4 (7.0)</td>
<td>15 (14.5)</td>
</tr>
<tr>
<td>Severe Malnutrition (&lt;=-3 SD)</td>
<td>23 (40.4)</td>
<td>27 (26.2)</td>
</tr>
<tr>
<td>Moderate Malnutrition (-2 to -3 SD)</td>
<td>38 (67.3)</td>
<td>20 (19.4)</td>
</tr>
<tr>
<td>Isolated Stunting, N (%)</td>
<td>20 (35.1)</td>
<td>21 (20.2)</td>
</tr>
<tr>
<td>Antibiotics given within 1 hr of admission</td>
<td>0% (0/57)</td>
<td>16% (17/103)</td>
</tr>
</tbody>
</table>

** Figure 2: Mortality Rate Pre- and Post-Protocol

** Table 2: Secondary Clinical Outcomes

| Primary Outcome | Mortality was not significantly different at 32.17% pre- and 34.99% post-protocol, p=0.72 (Figure 2), but was higher in children with acute on chronic malnutrition (Figure 3).

Secondary Outcomes: There were higher rates of fluid overload (31.47% vs. 54.05%, p<.001), heart failure (3.5% vs. 10.27%, p=0.02) and a longer LOS (96 hrs vs. 120 hrs, p=0.16) in the post-protocol cohort, especially in severely malnourished children (Table 2).

** Protocol Compliance: Both cohorts had similar rates of antibiotic administration (16.08% vs. 12.43%, p=0.42), but the post-protocol cohort received more blood transfusions (9.09% vs. 31.89%, p<0.001) (Figure 4).

** Logistic Regression:

Mortality Risk factors: malnutrition (WAZ), low hematocrit, and meeting severe sepsis criteria.

Fluid overload risk factors: being post-protocol, low hematocrit, and receiving a blood transfusion.

** Discussion

A pediatric sepsis protocol in this resource-limited setting did not improve survival and may have worsened clinical outcomes, especially in severely malnourished children. This may be due to poor protocol compliance and/or increased transfusions. Future studies should focus on: potential roadblocks, tailoring the protocol to available resources, and educating all members of the treatment team.

**References


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