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Prognostic Value of Serum Glucose Level in Septic Children in PICU

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ABSTRACT

Introduction

Pediatric sepsis is a major cause of morbidity and mortality. Abnormal blood glucose is linked with higher mortality, increased requirement for mechanical ventilation and inotropic support. This study is aimed to determine the prognostic value of serum glucose level in sepsis children in PICU.

Methods

This retrospective study was performed in the Pediatric Intensive Care Unit (PICU) of Kanti Children's Hospital with diagnosis of Sepsis from April 2024 to September 2024 with age ranging from 1 month to 14 years. The data was collected from the record section. The outcome of sepsis in the form of discharge or death during the hospital stay, length of hospital stay, use of ionotropic support, mechanical ventilation and blood sugar level were tabulated and the data analysis was done by SPSS version 21.

Results

Among 53 patients enrolled, 21 were male and 22 were female with male to female ratio of 1.4. The median age of the patient is 2.5±4.46 years. The median length of hospital stay was 7± 5days. There was no statistical significance in the length of PICU stay, use of ionotropic support and septic shock in patients with abnormal blood glucose. However, it was significantly associated with mortality (p value 0.009) and use of mechanical ventilator (p value 0.09).

Conclusion

Our study highlights that abnormal blood glucose level in pediatric sepsis is significantly associated with increased mortality and a greater need for mechanical ventilation. However, no significant relationship was observed between abnormal blood glucose, length of PICU stay and ionotropic support.

Keywords
Pediatric; hypoglycemia; prognosis; sepsis

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INTRODUCTION

Sepsis, a potentially fatal illness brought on by a dysregulated host response to infection.[1] It continues to be a major source of morbidity and mortality, especially in newborns, young children, and the elderly.[2] Even in high-income nations, pediatric sepsis still has a high death rate of about 11 % despite advancements in care;[3] however, the mortality in Nepal at Kanti Children Hospital is 26.4%[4] with a notable gap of around two times.

Hyperglycemia in sepsis is caused by a neuroendocrine response triggered by pro-inflammatory cytokines (Interleukin (IL)-1, IL-6, and Tumor necrosis Factor (TNF-α).[5] Insulin resistance is caused by elevated catecholamines and pro-inflammatory cytokines, which also promote hepatic gluconeogenesis and glycogenolysis while hindering insulin-mediated glucose absorption in skeletal muscle.[6] Although the exact causes of hypoglycemia in sepsis are unknown, they could be due to inadequate nutritional availability, decreased gluconeogenesis, increased glucose consumption, or glycogen depletion.[7]

The outcomes of patients in the pediatric intensive care unit (PICU) may be considerably impacted by these blood-glucose abnormalities. Higher mortality, increased requirement for breathing, use of inotropic support, and serious systemic consequences such as cardiac arrhythmias and autonomic dysfunction are all linked to (hypoglycemia and hyperglycemia) abnormal glucose level in particular.[7,8] Random blood-glucose (RBG) measurement is a quick, easy, and affordable technique that can be used as an early prognostic tool in critically unwell septic children; as such, it is crucial for routine monitoring and prompt correction in the PICU setting.[9] So, our study aimed to determine the prognostic value of serum glucose level in sepsis children in PICU.

METHODS

This was a retrospective study performed in the PICU of Kanti Children's Hospital with diagnosis of Sepsis, from April 2024 to September 2024. This study was approved by the Institutional Review committee of Kanti Children Hospital. The study included sepsis patients with age ranging from 1 month to 14 years. All the data were recorded from the record section of the hospital. Informed consent was not taken because this was a retrospective study using clinical data.

Sepsis was diagnosed on the basis of clinical and laboratory findings. Sepsis involves a systemic inflammatory response syndrome (SIRS) in presence of infection. It was based on the 2005 International Pediatric Sepsis Consensus Conference. Any two of the clinical findings including core temperature >38°C or <36°C, tachycardia or bradycardia not due to an external stimulus and tachypnea not caused by neuromuscular disease and laboratory finding include leucocyte count abnormal for age or over 10% immature neutrophils[10, 11] along with culture report were taken for the diagnosis. The exclusion criteria were other causes apart from sepsis, hypoglycemia and Diabetes Mellitus. Pediatric hypoglycemia was defined as blood glucose <70mg% by American Diabetes Association (ADA) and hyperglycemia as random blood sugar of >200mg%, was taken in the study[12].

A comprehensive medical history and examination findings were recorded from admission file just after admission. It included demographic profile, clinical features, comorbidities, laboratory parameters of the individual patient. The outcome of the patients in the form of discharge or death within the hospital stay were noted. The clinical variables recorded include fever, diarrhea, vomiting, headache, cough, shortness of breath, altered sensorium, seizure, burning micturation, hematuria and oliguria. The recorded examination findings include pulse, blood pressure, respiratory rate, temperature, general physical examination and systemic examination findings. Initial laboratory tests at the time of admission or discharge note including blood glucose level, complete blood count with differential, C-reactive protein, arterial blood gases, liver function tests, kidney function tests, coagulation profile, and cultures were recorded. The outcome of sepsis including review of body systems, PICU length of stay, use of mechanical support, use of ionotropes, residual morbidities at PICU, discharge, and mortality were recorded.

Following retrospective data collection, the dataset was cleaned, coded, and subsequently entered into the SPSS Statistics software version 27, for analysis. Categorical variables were summarized using frequencies and percentages, while continuous variables were expressed as mean ± standard deviation or median (interquartile range [IQR]), based on the distribution. For non-parametric data, associations were assessed using the Spearman rank correlation coefficient and the Mann–Whitney U test, as appropriate. A p-value of less than 0.05 was considered indicative of statistical significance.

RESULTS

Out of a total of 53 patients 21 were male and 22 were female with male to female ratio of 1.4. The median age of the patient is 2.5±4.46 years. The most common clinical condition causing sepsis was found to be pneumonia in 9 (17.1%) patients. Other clinical conditions were UTI, meningitis, autoimmune disease, sinusitis and acute gastroenteritis. The cause was unknown in 26 patients (49.4%). The most common symptom

Table 1. Comparison between RBS group and gender variables

Gender	Blood glucose level (mg%)			Total
	<70	70-200	>200	
Male	14 (45.2%)	17 (54.8%)	0 (0%)	31 (100%)
Female	7 (31.8%)	14 (63.6%)	1 (4.5%)	22 (100%)

of sepsis was found to be fever in 50 (94.4%) patients and the other symptoms enrolled in the study were cough, shortness of breath, diarrhoea, vomiting, headache, burning micturation and altered sensorium. The median length of hospital stay was 7± 5days.

Among 53 patients included in the study 21 had blood glucose levels less than 70mg/dl (39.6%), 31 had blood glucose levels between 70-200mg/dl (58.3%) and 1 had blood glucose levels above 200 mg/dl (1.9%). (Table 1) The baseline characteristerics of the patients is given in Table 2.

Out of a total of 53 patients 39 (73.6%) were survivors and 14 (26.4%) were non-survivors. Among survivors, 27(69.2%) had blood glucose between 70-200mg/dl, 12(30.8%) had blood glucose <70mg/dl and none had blood glucose >200mg/dl, while among non-survivors, 9 (64.3%) patients had blood glucose less than 70mg/dl and 1 had blood glucose >200mg%.This shows a statistical significant difference in abnormal blood glucose in the form of hypoglycemia and mortality (p=0.009). Similarly hypoglycemia was associated with need of mechanical ventilation (p value 0.086) (Table 3). There was no statistical difference in the length of PICU stay (p-value 0.548), use of ionotropic support (p-value 1) and septic shock (p-value1) in patients with abnormal blood glucose.

Table 2. Baseline characteristics and laboratory investigations

Baseline characteristics	Median	Interquartile range
Hemoglobin(mg/dL)	10.4	8.6-11
Creatinine (mg/dL)	0.4	0.3-0.6
CRP (mg/dL)	1.5	1.5-12.6
ESR (mm/hr)	50	27.5-62.5
Length of PICU stay (days)	4	2-6

DISCUSSION

Sepsis is a significant cause of disease and death in children. Glucose homeostasis varies among children with sepsis and septic shock.[13] Therefore, we aimed to detect the relation between critically ill septic patients and their initial RBG. In this study male were found to be more effected than female which is similar to the study done by Ghimire.[14] The mean age of the patient is 41.97 months, which is similar to study done by Kaur G et al.[15]The lower age may be due to low immunity in younger age. The most common clinical condition causing sepsis was found to be pneumonia in 17.1% patients which is consistent with the other studies.[16,17] The most common symptom in this study was found to be fever which is similar to study done by Bhatta et al.[18] The mean length of hospital stay was 4.64 days. In most of the other studies the length of hospital stay was longer as compared to this study.[17,19] The reason behind is few patients are severely diseased like septic shock (24%), use of ionotropic support (24%) and patient on mechanical Ventilation (18%) as compared to other studies.

Our study demonstrates that hypoglycemia in pediatric patients with sepsis admitted to the intensive care unit is significantly associated with increased risks of mortality. Sepsis is a complex syndrome characterized by physiologic, pathologic, and biochemical abnormalities induced by infection.[16] It remains a major cause of pediatric morbidity and mortality, accounting for up to 30% of PICU admissions and with reported mortality rates exceeding 10%.[19,20] Although the exact causes of

Table 3. Comparison of mortality, septic shock, and need for mechanical ventilation with blood glucose level

Characteristics	Blood glucose level (mg%)			p-value
	<70	70-200	>200	
Survivors, n (%)	12(30.8%)	27(69.2%)	0(0.0%)	0.009
Non-survivors, n (%)	9(64.3%)	4(28.6%)	1(7.1%)	0.009
Septic shock, n (%)	5(38.5%)	8(61.5%)	0(0.0%)	1
Mechanical ventilation, n (%)	6(54.5%)	4(36.4%)	1(9.1%)	0.086
Use of ionotropic Support n (%)	5(38.5%)	8(61.5%)	0(0.0)	1

hypoglycemia in sepsis are unknown. Some of the postulations are inadequate nutritional availability, decreased gluconeogenesis, increased glucose consumption, or glycogen depletion.[7]

Consistent with findings reported by Mohamed et al.[9], our study identified hypoglycemia as a significant prognostic factor for mortality in pediatric patients with sepsis. Low blood glucose levels in intensive care unit patients in the very early phase of sepsis have already been shown to be significantly related to mortality before using insulin in a study done by Mitsuyama et al.[19] A systematic review and meta-analysis by Wang et al. further reinforced these findings, highlighting that spontaneous early hypoglycemia was significantly linked to poor clinical outcomes in sepsis.[20, 21] Similarly, Mitsuyama et al. observed that both moderate and severe hypoglycemia were independently associated with increased mortality in critically ill septic patients.[19] The potential pathophysiologic mechanisms underlying hypoglycemia is associated sepsis include dysregulation of adrenal hormones (e.g., cortisol and adrenaline), impaired hepatic gluconeogenesis, increased peripheral glucose utilization, vasoconstriction with altered perfusion, and heightened inflammatory responses mediated by cytokine release.[20,21] A shortage of glucose for cellular respiration can lead to a shortage of adenosine triphosphate and subsequent energy failure which finally leading to mortality.[22]

In contrast to prior studies,[23] we did not observe a statistically significant relationship between abnormal blood glucose levels and the duration of PICU stay. Mahamed et al. reported a positive correlation between random blood glucose levels and PICU length of stay,[9] and Bagshaw et al. demonstrated that initial hypoglycemia predicted prolonged PICU admissions,[24] our findings did not align with these results. However, consistent with Bagshaw et al.[24] our analysis did reveal that patients with hypoglycemia-associated sepsis required mechanical respiratory support more frequently than their normoglycemic counterparts but stastistically non-significant.

Septic shock in most of the studies[26] was associated with increased mortality which was not found in this study. Similarly, use of ionotropic support was also not found to be statistically significant which is inconsistent with other studies.[25,26] The reason behind is that in this study only few patients had septic shock and use of ionotropic support which was timely managed.

This study has several limitations. First, it was conducted as a retrospective, observational analysis, which may be subject to selection bias and residual confounding. Second, the study was limited to a single-center cohort, which may restrict the generalizability of the findings. Future prospective, multicenter studies with larger sample sizes are needed to validate our results. Lastly, we were unable to delineate the underlying causes of hypoglycemia such as deficiencies in cortisol, glucagon, or other metabolic regulators due to limitations in available clinical data.

CONCLUSION

In conclusion, our study highlights that hypoglycemia in pediatric sepsis is significantly associated with increased mortality and a greater need for mechanical ventilation, however use of mechanical ventilation is not found to be statistically significant. No significant relationship was observed between abnormal blood glucose and the length of PICU stay, septic shock and use of ionotropic support. These findings call for further prospective, multicenter studies to better understand the underlying mechanisms and improve clinical outcomes.

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CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and/or publication of this article.

AUTHOR CONTRIBUTIONS

Study concept, design and methodology by Bulu Wagley. Literature review by Bulu Wagley and Askol Devkota. Data collection and data analysis by Bulu wagley. Research experiment, stastistical analysis and manuscript writing by Bulu Wagley, Sabin Rimal, Manisha Gaire, Samikshya Karki and Ajit Rayamajhi. All authors read and approved the final manuscript.

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