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Glucose-to-Potassium Ratio as a Prognostic Biomarker in Critically Ill Children: A Narrative Review

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ABSTRACT

Critically ill children in the Pediatric Intensive Care Unit (PICU) have a high risk of death, so simple and fast tools to identify those at greatest risk are needed. Scores such as PRISM, PELOD-2, PIM-3, and pSOFA require many variables, and their accuracy can depend on when they are calculated. The glucose-to-potassium ratio (GPR) has attracted attention as an alternative marker because it uses two routine blood tests available in most hospitals. This narrative review summarizes the physiological rationale and current evidence for GPR as a predictor of mortality in critically ill children. Literature from 2019 to 2026 was identified through non-systematic web-based searches of PubMed/PubMed Central, medRxiv, and publisher platforms. During severe stress, catecholamines, cortisol, and glucagon raise blood glucose, while insulin and catecholamines move potassium into cells and lower its serum level; together, these changes increase GPR and may reflect the severity of metabolic stress. In adults, a higher GPR has been linked to higher mortality in traumatic brain injury, intracerebral hemorrhage, ischemic stroke, acute aortic dissection, and thoracoabdominal trauma, although results in sepsis are conflicting. Evidence in children is very limited, with only one small study in severe traumatic brain injury identified. Differences in cut-off values and units, insulin therapy, and stress hyperglycemia complicate interpretation. GPR is a promising low-cost marker that merits evaluation as a complement to existing scores in the PICU. Prospective multicenter studies in children are needed to define reliable cut-offs and to test whether GPR adds value beyond existing scores.

Keywords: glucose-to-potassium ratio; pediatric intensive care unit; critical illness; mortality prediction; biomarker

INTRODUCTION

Critical illness in children is a serious global health problem. It happens when a child has a severe illness, injury, or complication after surgery that makes the body unstable and needs close monitoring and immediate treatment, usually in the Pediatric Intensive Care Unit (PICU). Common causes include severe infection, major trauma, metabolic disorders, and failure of several organs. In Indonesia, a study in Banda Aceh found that respiratory dysfunction was the most frequent cause of critical illness in children, and about one in five patients died [1]. Globally, child deaths have fallen over the past three decades, from 12.8 million under-five deaths in 1990 to 4.8 million in 2023, but the number is still high [2]. These figures cover all under-five deaths rather than PICU deaths, but they show the scale of the burden of severe childhood illness.

Because children in the PICU can worsen quickly, clinicians need tools that estimate the risk of death early and accurately. Several clinical scoring systems are used for this purpose, including the Pediatric Risk of Mortality (PRISM), Pediatric Logistic Organ Dysfunction-2 (PELOD-2), Pediatric Index of Mortality-3 (PIM-3), and pediatric Sequential Organ Failure Assessment (pSOFA). These scores perform reasonably well. For example, a meta-analysis reported good, pooled discrimination for PRISM-III/IV, with a summary area under the curve (AUC) of 0.84 [3].

However, some of them require many clinical and laboratory variables, and the accuracy of scores that are recalculated over time, such as pSOFA, can depend on the time of assessment [4]. This makes a simpler marker that can be obtained quickly at the bedside attractive.

One marker that has recently drawn attention is the glucose-to-potassium ratio (GPR), also called the stress index. It is calculated from blood glucose and serum potassium, two tests that are routinely done in almost all hospitals, so it is low-cost and easy to obtain. The idea behind GPR is that severe stress changes both values in opposite directions. Stress hormones such as catecholamines, cortisol, and glucagon raise blood glucose, while insulin and catecholamines push potassium into cells, which lowers its level in the blood [5]. A high GPR may therefore reflect the degree of metabolic stress in a critically ill patient.

In adults, a higher GPR has been associated with higher mortality in several conditions, such as traumatic brain injury [6], ischemic stroke [7], and acute aortic dissection [8]. The results are not consistent, however. One study in sepsis and septic shock found that GPR did not significantly predict death [9]. Reported cut-off values also differ between studies, and factors such as insulin therapy and stress-induced hyperglycemia can influence the ratio. Most importantly, almost all of this evidence comes from adults, and it is still unclear whether the same findings apply to children whose bodies respond differently to illness.

Therefore, this narrative review aims to summarize the physiological rationale and the current evidence for GPR as a prognostic biomarker in critically ill children. We also discuss its limitations and identify gaps that future research should address.

LITERATURE SEARCH STRATEGY

This narrative review updates and expands the literature review chapter of the first author's undergraduate thesis (Faculty of Medicine, Universitas Airlangga, 2026). Additional searches were conducted on 26 October 2026 through web-based searching of sources indexed in PubMed/PubMed Central, the medRxiv preprint server, and publisher platforms (Elsevier, Springer, Frontiers, Nature Portfolio, and PLOS). We used combinations of the keywords "glucose-to-potassium ratio", "glucose-potassium ratio", "stress index", "mortality", "prognosis", "critical illness", "intensive care", "pediatric", "children", "neonates", "sepsis", and "cardiac surgery". Sources on the physiology of glucose and potassium and on PICU scoring systems came mainly from the thesis literature review, and several of them (for example, reports of PRISM, PIM-3, PELOD-2, and pSOFA performance) were checked against the original publications during this update. The sources included in this review were published between 2019 and 2026, with one exception: an earlier foundational study on glycemic variability that is cited in its original form [10]. The search was not systematic and did not include Embase or Scopus, so relevant studies may have been missed.

The core search string, written in PubMed syntax and adapted to the other sources, was: ("glucose-to-potassium ratio"[tiab] OR "glucose potassium ratio"[tiab] OR "glucose/potassium ratio"[tiab] OR "stress index"[tiab]) AND (mortality[tiab] OR prognosis[tiab] OR "critical illness"[MeSH Terms] OR "critically ill"[tiab] OR "intensive care"[tiab]) AND 2019:2026[dp]. For evidence in children, the following block was added with AND: (child*[tiab] OR pediatric*[tiab] OR paediatric*[tiab] OR infant*[tiab] OR neonat*[tiab]). The physiology and scoring-system sections were searched with separate, narrower terms, for example "stress hyperglycemia" AND "critically ill children"; (hyperkalemia OR hypokalemia) AND "intensive care"; and (PRISM OR "PIM-3" OR "PELOD-2" OR pSOFA) AND mortality AND (child* OR pediatric*).

We included articles that (1) studied the glucose-to-potassium ratio in critically ill patients, either children or adults, with mortality or prognosis as an outcome, or (2) described the physiology or clinical significance of glucose and potassium disturbances in critical illness, or (3) described clinical scoring systems used to predict mortality in the PICU. Search queries were written in English, and articles in English and Indonesian were considered. Animal studies and case reports were not considered. Where the full text was not accessible, data was taken from the abstract.

Titles and abstracts were screened, and the full text of potentially relevant articles was read where available. Findings were summarized descriptively and grouped by theme: physiological background, mechanisms of GPR, evidence in adults, evidence in children, and limitations. As this is a narrative review, we did not perform a formal quality appraisal of the included studies or a meta-analysis. The structure and reporting of this review were guided by the Scale for the Assessment of Narrative Review Articles (SANRA) [11], which covers six elements: justification of the importance of the topic, statement of aims, description of the literature search, referencing, scientific reasoning, and appropriate presentation of data. Each element is addressed in the corresponding sections of this manuscript.

PHYSIOLOGICAL BACKGROUND

Glucose in critical illness

Glucose is the body's main source of energy. Cells break it down through glycolysis to produce ATP, which powers muscle contraction, nerve signals, active transport across cell membranes, and tissue repair. Extra glucose is stored as glycogen, mainly in the liver and muscle. During stress, such as severe infection, liver glycogen is broken down and released as glucose to keep blood glucose stable, whereas muscle glycogen is used mainly within the muscle itself [12]. Glucose is also linked to potassium balance, because the ATP-dependent transport that keeps potassium inside cells relies on a steady energy supply.

Stress hyperglycemia is common in critically ill children. Stress hormones and inflammatory cytokines cause insulin resistance and increase glucose production, so blood glucose rises [13]. This rise was once seen as useful fuel for the "fight-or-flight" response, but many studies now link it to worse outcomes, including in children [13]. Intensive care unit (ICU) treatments such as parenteral nutrition, catecholamines, and corticosteroids can make it worse. Tight glucose control with insulin has produced inconsistent results and sometimes caused harm through hypoglycemia [13]. In a study of 481 critically ill children aged 28 days to 14 years, 28.9% had abnormal glucose levels on admission: 23.9% had hyperglycemia and 5% had hypoglycemia, and 11.5% of those with dysglycemia died during intensive care [14].

Hypoglycemia is less frequent but also dangerous. It is often a sign of severe illness and has been linked to higher short- and long-term mortality in the PICU [15]. In a secondary analysis of the PEPaNIC trial (N = 1,440; hypoglycemia defined as glucose below 40 mg/dL), hypoglycemia was associated with mortality in the PICU at 90 days and up to four years after admission, but these associations were no longer significant after adjusting for other risk factors, which suggests that hypoglycemia is at least partly a marker of illness severity. Children who had hypoglycemia also scored lower on executive function tests four years later [15].

Potassium in critical illness

Potassium is the main intracellular cation (positively charged ion). It maintains the resting membrane potential and allows electrical signals to travel through nerves, skeletal muscle, and the heart. Its level is controlled in two ways: movement between the blood and cells, which is influenced by insulin, β2-adrenergic activity, and acid-base status, and excretion by the kidneys, which depends on aldosterone, sodium delivery to the distal tubule, and adequate kidney perfusion [16]. In the ICU, intravenous fluids, diuretics, and insulin can all change these processes, so potassium needs close monitoring.

Hyperkalemia is usually defined as serum potassium above about 5.5 mmol/L (the usual normal range is about 3.5–5.5 mmol/L). In newborns, especially premature babies, levels up to 6.5 mmol/L can still be normal because the kidneys are immature. Severe hyperkalemia (above 7.0 mmol/L, or above 6.5 mmol/L with ECG changes) can cause slow heart rate, AV block, and cardiac arrest [17]. In the PICU, it is associated with acute kidney injury and blood transfusion [18], and hemolyzed samples can give falsely high results.

Besides the absolute value, unstable potassium levels during treatment also matter. In critically ill children, variability in electrolytes was associated with in-hospital mortality, and mortality followed a U-shaped pattern for potassium, lowest at about 3.5–5.0 mmol/L and higher outside this range; patients with the greatest variability had markedly higher odds of death [19].

Hypokalemia means serum potassium below 3.5 mmol/L. It is a common electrolyte disorder in critically ill children: in a PICU study from Karachi, 26 of 85 children (30.6%) with an electrolyte imbalance had hypokalemia [20]. Causes include potassium loss through vomiting or diarrhea, drugs such as loop diuretics, thiazides, and β2-agonists, and shifts of potassium into cells caused by insulin, metabolic alkalosis, or high sympathetic activity [21]. It can lead to muscle weakness, ileus, and dangerous heart rhythm problems, and it can develop quickly, so continuous monitoring is recommended [22].

Linking glucose and potassium

In severe illnesses, the same stress response tends to push glucose up and potassium down at the same time. This is the basis for combining both values into one ratio, which is discussed in the next section.

PATHOPHYSIOLOGICAL RATIONALE OF GPR

How severe stress changes glucose and potassium

The glucose-to-potassium ratio (GPR) reflects how two parts of the body's stress response interact: energy metabolism (glucose) and electrolyte balance (potassium). In healthy people, both are tightly controlled by the endocrine and autonomic nervous systems. In severe illnesses such as sepsis, shock, major injury, or multiple organ failure, this balance is disturbed, and GPR can rise.

In the early phase of stress, the body releases catecholamines, cortisol, and glucagon. These hormones increase glucose production through glycogen breakdown (glycogenolysis) and the creation of new glucose (gluconeogenesis), which leads to hyperglycemia. At the same time, insulin and catecholamines (through β2-adrenergic receptors) stimulate the Na^+/K^+-ATPase pump, which moves potassium from the blood into cells. As a result, serum potassium falls even though total body potassium may not change [5]. Alkalosis, as well as potassium loss through urine or the gut, can lower potassium further. The combination of high glucose and relatively low potassium produces a high GPR, which is often seen as a sign of severe metabolic dysfunction and extreme activation of the stress system (Figure 1).

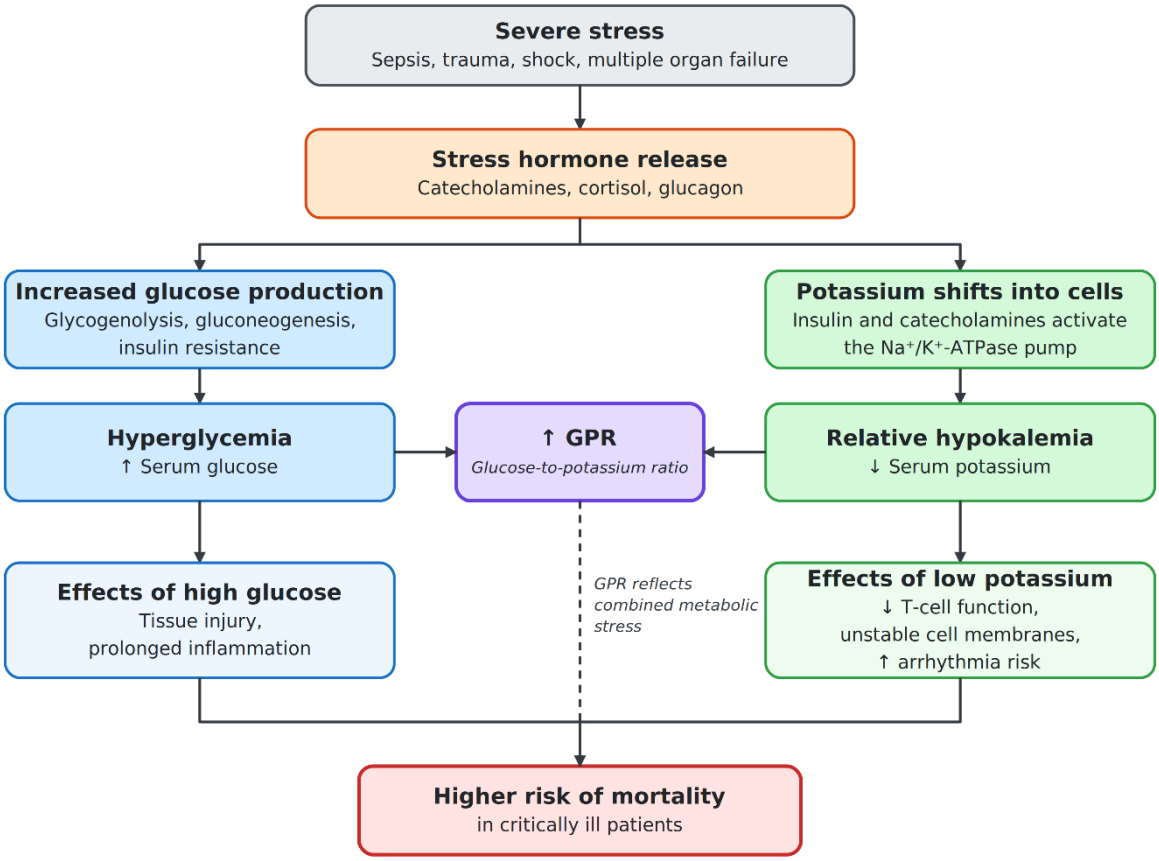


FIGURE 1: Proposed Pathophysiological Mechanism Linking Severe Stress to an Elevated Glucose-To-Potassium Ratio (GPR) in Critical Illness. Stress hormones increase glucose production, while insulin and catecholamines shift potassium into cells, producing hyperglycemia and relative hypokalemia. GPR combines both changes and may reflect the severity of metabolic stress. Created by the authors based on [5] and [7].

Why the combination may matter for prognosis

Each part of the ratio can harm the patient in its own way. Hyperglycemia can worsen tissue injury and prolong inflammation. Low potassium can weaken T-cell function, make cell membranes less stable, and increase the risk of dangerous arrhythmias. One study in ischemic stroke suggested that GPR captures both metabolic stress from high glucose and impaired immune cell function from low potassium [7].

A preprint analysis of adult patients with sepsis reported that GPR discriminated mortality better than glucose or potassium alone [23]. In the PICU, glucose and potassium can change very quickly because of severe infection, circulatory problems, insulin or diuretic therapy, and kidney dysfunction. By combining both values, GPR may therefore give a more integrated picture of metabolic stress than monitoring either one separately, although this is a hypothesis that has not yet been tested in children. This is why it has been proposed as an early clinical marker of illness severity and mortality risk in critically ill patients.

Conceptual limitations

The ratio also has weaknesses. Potassium disturbances in both directions have been linked to death in critically ill patients: in a large cohort of ICU patients with sepsis, higher potassium (above 4.4 mmol/L, a value still within the usual normal range) was associated with greater mortality [24], and early hyperkalemia increased the risk of death in an ICU database study [25]. A high potassium level lowers GPR, so the ratio may not capture risk in these patients. In addition, different glucose and potassium combinations can produce the same GPR value, and treatments such as insulin or diuretics can change the ratio without reflecting disease severity. These issues are discussed further in the section on limitations and confounding factors.

EVIDENCE OF GPR AS A MORTALITY PREDICTOR

Evidence from adult populations

Most studies on GPR have been done in adults, especially in acute neurological and cardiovascular emergencies. In severe traumatic brain injury (TBI), a higher GPR independently predicted 30-day mortality, with an area under the curve (AUC) of 0.777, similar to the Glasgow Coma Scale [6]. In a Japanese cohort of severe TBI, a GPR of 50 or higher at arrival was associated with about four-fold higher odds of death or a vegetative state [26]. In ICU patients with intracerebral hemorrhage, a higher GPR was linked to higher mortality at 30 days, 90 days, and one year, even after adjusting for age, sex, and comorbidity [27]. In ischemic stroke, a higher GPR at admission was associated with a higher risk of death within 30 days, and the relationship was linear [7]. In acute type A aortic dissection, patients with a GPR above the cohort median (1.74) had higher in-hospital mortality after surgery, independent of lactic acidosis and mechanical ventilation [8].

GPR also predicted the need for surgery and death in blunt thoracoabdominal trauma (AUC 0.854) [28], and in a cohort of 3,157 coronary care unit patients, a higher GPR was an independent predictor of in-hospital mortality (odds ratio 1.015 per unit); however, adding GPR to a clinical model raised the AUC only from 0.835 to 0.842 [29]. Together, these studies show a tendency toward higher mortality with higher GPR across very different conditions (Table 1). However, most of them are retrospective, and the signal is not universal: in a cohort of 764 patients with isolated blunt head trauma, GPR was not significantly associated with mortality ($p = 0.261$) [30].

Inconsistent findings

The evidence is not uniform. In patients with sepsis and septic shock, GPR did not significantly predict mortality ($p = 0.324$), and the Acute Physiology and Chronic Health Evaluation (APACHE) II score performed better [9]. In contrast, an analysis of the Medical Information Mart for Intensive Care IV (MIMIC-IV) database in ICU patients with sepsis found that a higher GPR was associated with higher short- and long-term mortality [31]. A preprint of another MIMIC-IV analysis in sepsis reported the opposite direction, with a higher GPR (highest tertile, ≥34.69) associated with lower mortality, although GPR still discriminated better than glucose or potassium alone [23]. Results in sepsis are therefore conflicting. The two MIMIC-IV analyses were drawn from the same database, so the difference may reflect how GPR was calculated, how patients were grouped, and how the analysis was designed rather than a true difference between patients. In the preprint, the highest GPR tertile also contained many more patients with diabetes (58.0% vs 22.3% in the lowest tertile), which may raise GPR through chronic hyperglycemia rather than acute stress [23]; the analysis is also a preprint that has not been peer-reviewed.

More generally, the value of GPR may depend on the type of critical illness. In sepsis, glucose and potassium can be disturbed by many causes at once, such as infection, organ dysfunction, and treatment, which may dilute the signal. Studies also differ in when GPR was measured, how it was calculated, and which cut-off was used.

Evidence in children

Evidence in children is very limited. In our search, we identified only one published study that evaluated GPR for mortality prediction in children, and it did not involve a general PICU population. A search that combined GPR or the stress index with pediatric, neonatal, sepsis, and cardiac surgery terms did not find any other pediatric study as of October 2026. The study was a cross-sectional analysis at a Brazilian trauma reference center that included 40 children with severe TBI (mean age 9 years) who were admitted between 2016 and 2023. GPR was calculated from glucose and potassium values taken in the first 24 hours after injury. Hyperglycemia was present in 33% and hypokalemia in 58% of the children; mortality was 23%, the AUC was 0.71, and a cut-off of 50 gave a negative predictive value of 91%. The authors described this as moderate performance, with the cut-off mainly useful to identify children at lower risk of death [32].

This study is small, comes from a single center, and is limited to one diagnosis, so its findings cannot be generalized to the wider PICU population, which includes sepsis, respiratory failure, and many other conditions. Related pediatric studies support the building blocks of GPR, such as abnormal glucose on PICU admission [14] and the high frequency of potassium disturbances [20], but they do not test the ratio itself. Therefore, the prognostic value of GPR in a general PICU cohort remains unknown.

TABLE 1: Summary of Studies on GPR and Mortality in Critically Ill Patients.

Study	Population/setting	Outcome	Main finding
Zhou et al. [6]	Adults, severe TBI	30-day mortality	Independent predictor; AUC 0.777, comparable to GCS
Shibata et al. [26]	Adults, severe TBI (n = 264)	In-hospital death or vegetative state	GPR of 50 or higher associated with poor outcome (OR 4.08)
Liu et al. [27]	Adults, intracerebral hemorrhage, ICU (n = 2,018)	30-day, 90-day, 1-year mortality	Higher GPR linked to higher mortality after adjustment
Lu et al. [7]	Adults, ischemic stroke	30-day mortality	Higher admission GPR linked to higher mortality; linear relationship
Chen et al. [8]	Adults, acute type A aortic dissection, surgery (n = 272)	In-hospital mortality	GPR above the cohort median (1.74) was an independent predictor
Turan and Şahin [28]	Adults, blunt thoracoabdominal trauma	Surgical intervention, mortality	AUC 0.854
Ünal and Dogan [30]	Adults, isolated blunt head trauma (n = 764)	Mortality	No significant association ($p = 0.261$)

Study	Population/setting	Outcome	Main finding
Demir et al. [29]	Adults, coronary care unit (n = 3,157)	In-hospital mortality	Independent predictor; model AUC 0.842 vs 0.835 without GPR
Güler et al. [9]	Adults, sepsis and septic shock (n = 175)	In-hospital mortality	Not significant (p = 0.324); APACHE II better
Lou et al. [31]	Adults, sepsis, ICU (MIMIC-IV)	Short- and long-term mortality	Higher GPR associated with higher mortality
Kang and Yu [23] (preprint)	Adults, sepsis, ICU (MIMIC-IV)	28-day to 1-year mortality	Higher GPR (highest tertile, ≥34.69) associated with lower mortality; AUC 0.677 at 28 days
de Oliveira et al. [32]	Children, severe TBI, Brazilian trauma center (n = 40)	In-hospital mortality	AUC 0.71; cut-off 50 gave NPV 91%

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; AUC, area under the curve; GCS, Glasgow Coma Scale; GPR, glucose-to-potassium ratio; ICU, intensive care unit; MIMIC-IV, Medical Information Mart for Intensive Care IV; NPV, negative predictive value; OR, odds ratio; TBI, traumatic brain injury.

GPR IN THE CONTEXT OF ESTABLISHED SCORING SYSTEMS

Clinical scores are still the most widely used tools for predicting death in the PICU. A meta-analysis of 29 studies found good, pooled discrimination for the three most widely studied scores, although the certainty of evidence was low to moderate. PRISM-III/IV had a pooled sensitivity of 0.78, a pooled specificity of 0.75, and a summary AUC of 0.84; PIM-3 had 0.75, 0.76, and 0.82; and PELOD-2 had 0.78, 0.75, and 0.83 [3] (Table 2). The Pediatric Risk of Mortality (PRISM) score uses physiological data from the first 24 hours after admission [4]. The Pediatric Logistic Organ Dysfunction-2 (PELOD-2) score measures the degree of multiple organ dysfunction, and the Pediatric Index of Mortality-3 (PIM-3) is intended for risk estimation around the time of admission. The pediatric Sequential Organ Failure Assessment (pSOFA) can be recalculated over time, and its accuracy changes with the time of assessment: in a prospective study of 151 children, pSOFA at 72 hours predicted 28-day mortality better (AUC 0.870) than pSOFA at admission (AUC 0.765) or PRISM III (AUC 0.701) [4]; however, PRISM III was calculated within the first 24 hours, so this comparison is not like-for-like. Performance therefore varies between settings and time points.

These scores are well studied, but PRISM and PELOD-2 need many clinical and laboratory variables, usually the worst values over the first 24 hours, and some scores (such as pSOFA) perform better after a period of observation. PIM-3 is available earlier, but PRISM and PIM were designed mainly for risk adjustment and benchmarking of PICU populations rather than for decisions about individual children.

GPR has a different profile. It uses only two routine blood tests that are available in almost every hospital, so it is quick, low-cost, and easy to repeat. In adult studies, GPR remained an independent predictor of mortality after adjustment for lactic acidosis and mechanical ventilation [8] and for age, sex, and comorbidity [27]. An independent association does not by itself show added predictive value: in a coronary care unit cohort, adding GPR to a clinical model raised the AUC only from 0.835 to 0.842 [29]. However, GPR is a single laboratory ratio, not a scoring system. It does not capture organ dysfunction, age, or diagnosis; it can be influenced by insulin therapy and stress hyperglycemia, and it has not been validated in general PICU populations. Therefore, current evidence supports GPR, at most, as a possible complement to established scores that still need to be tested in children, rather than as a replacement. Future studies should compare GPR directly with PRISM, PELOD-2, and PIM-3 in the same cohort, and test whether adding GPR to these scores improves prediction.

TABLE 2: Comparison of GPR with Established PICU Mortality Prediction Tools.

Tool	Main focus	Reported performance	Practical notes
PRISM-III/IV	Physiological status within 24 h of admission	Summary AUC 0.84; sensitivity 0.78; specificity 0.75 [3]. AUC 0.701 in one single-center study [4]	Widely used in PICUs; needs many variables
PELOD-2	Multiple organ dysfunction	Summary AUC 0.83; sensitivity 0.78; specificity 0.75 [3]	Reflects organ failure burden
PIM-3	Mortality risk around PICU admission	Summary AUC 0.82; sensitivity 0.75; specificity 0.76 [3]	Intended for early risk estimation; uses a limited set of variables

Tool	Main focus	Reported performance	Practical notes
pSOFA	Organ dysfunction; can be repeated over time	AUC 0.765 at admission and 0.870 at 72 h in one single-center study [4]	Accuracy depends on time of assessment
GPR	Metabolic stress (glucose and potassium)	Pediatric data are very limited (AUC 0.71 in severe pediatric TBI [32])	Two routine tests; low-cost and repeatable; not validated in general PICU populations

Abbreviations: AUC, area under the curve; GPR, glucose-to-potassium ratio; PELOD-2, Pediatric Logistic Organ Dysfunction-2; PICU, pediatric intensive care unit; PIM-3, Pediatric Index of Mortality-3; PRISM, Pediatric Risk of Mortality; pSOFA, pediatric Sequential Organ Failure Assessment; TBI, traumatic brain injury.

LIMITATIONS AND CONFOUNDING FACTORS

Although GPR is attractive because it is simple, several issues limit how it can be interpreted and used.

Different cut-off values and ways of calculating GPR

Reported cut-offs and thresholds vary widely between studies. For example, the aortic dissection study [8] divided patients at the cohort median (1.74), the sepsis preprint [23] used a tertile boundary of 34.69 (neither is an optimized cut-off), and a cut-off of 50 was used in the pediatric TBI study [32], the same value reported in adults with severe TBI [26]. Part of this difference is probably due to units. Some studies calculate GPR by dividing glucose and potassium both in mmol/L [8], whereas others divide glucose in mg/dL by potassium in mmol/L [23]. Because glucose in mg/dL is about 18 times its value in mmol/L, the two methods differ about 18-fold: a GPR of 1.74 calculated in mmol/L corresponds to about 31 when glucose is in mg/dL, and a cut-off of 50 corresponds to about 2.8 when glucose is in mmol/L. Several reported thresholds may therefore be closer than they appear. The abstract of the pediatric TBI study [32] does not state its unit, although a cut-off of 50 is consistent with glucose in mg/dL. Studies also differ in when the blood sample was taken (on admission, within 24 hours, or later) and in the patient group, so cut-offs cannot simply be compared or transferred. A standard way of calculating and reporting GPR is needed before it can be used in practice.

Treatments and clinical conditions that change glucose and potassium

In the PICU, many treatments change glucose and potassium independently of how severe the disease is. Parenteral nutrition, catecholamines, and corticosteroids can raise blood glucose and make it harder to control [13]. Insulin lowers glucose but also pushes potassium into cells. Loop diuretics, thiazides, and β2-agonists can lower potassium, while acute kidney injury and blood transfusion are associated with high potassium [18,21]. A hemolyzed blood sample can give a falsely high potassium value, which would also falsely lower GPR. Pre-existing diabetes raises baseline glucose independently of acute stress. Diabetic ketoacidosis and other forms of metabolic acidosis raise glucose and shift potassium out of cells; potassium supplementation and potassium-containing fluids raise potassium; tissue breakdown (for example, rhabdomyolysis or tumor lysis) releases potassium, and delayed processing of samples lowers glucose and raises potassium; values from blood gas analyzers and laboratory analyzers may also differ. As a result, the same GPR value can mean different things in different patients, and GPR taken after treatment has started may reflect the treatment more than the illness (Table 3).

Variability and non-linear effects of glucose and potassium

GPR is usually calculated from a single measurement, but the way glucose and potassium change over time may matter as much as their level. A retrospective study of 3,252 adult ICU patients [10], as summarized in a recent review [33], found that mortality was much higher in the highest quartile of glucose variability than in the lowest (37.8% vs 12.1%). Potassium variability has also been reported as an independent predictor of 28-day mortality [34], and in critically ill children, mortality follows a U-shaped pattern, with higher risk at both low and high potassium [19]. In addition, higher potassium has been linked to higher mortality in ICU patients with sepsis [24], and hyperkalemia has been linked to higher mortality in general ICU patients [25]. Because a high potassium level lowers GPR, the ratio may look reassuring in these patients even though their risk is high. Tight glucose control with insulin has not consistently improved outcomes and has sometimes caused harm through hypoglycemia [13], and insulin also shifts potassium into cells, so treatment can change both parts of the ratio at once (Table 3).

Limits of the available evidence

Most evidence comes from adults, from retrospective and single-center studies, and from specific diseases such as brain injury, stroke, and aortic dissection. Even where several cohorts are available, as in adult TBI, a 2026 meta-analysis reported high heterogeneity (I^2 = 88% for the mortality comparison) and possible small-study effects [35]. The only pediatric study we found was small and limited to severe TBI. Critical illness in children is also very diverse, and normal values change with age. For example, the upper limit of normal potassium is higher in premature newborns (see above). Studies on GPR in children therefore need age-specific analysis, and results from adults cannot be applied directly.

TABLE 3: Factors That May Confound the Interpretation of GPR in the PICU.

Factor	Effect on glucose or potassium	Implication for GPR interpretation
Insulin therapy	Lowers glucose; shifts potassium into cells	May change both parts of the ratio at once
Dextrose, parenteral nutrition, catecholamines, corticosteroids	Raise blood glucose	May raise GPR without reflecting more severe disease
Loop diuretics, thiazides, β2-agonists	Lower potassium	May raise GPR
Acute kidney injury, transfusion	Raise potassium	May lower GPR despite high risk
Hemolyzed sample	Falsely high potassium	May falsely lower GPR
Pre-existing diabetes mellitus	Chronically higher baseline glucose, independent of acute stress	May raise GPR without reflecting acute illness severity
Diabetic ketoacidosis, other metabolic acidosis	Raises glucose (ketoacidosis); acidosis shifts potassium out of cells	May raise or lower GPR; interpret with acid-base status
Potassium supplementation, potassium-containing fluids	Raise potassium	May lower GPR independent of disease severity
Tissue breakdown (rhabdomyolysis, tumor lysis)	Release potassium from cells	May lower GPR despite high risk
Delayed sample processing; blood gas vs laboratory analyzer	Glucose falls, and potassium rises in unseparated samples; methods differ	May lower GPR; values from different methods are not interchangeable
Glucose or potassium variability	Not captured by a single value	A single GPR may miss risk
Age (especially neonates)	Different normal ranges	Cut-offs may not apply across ages

CLINICAL IMPLICATIONS AND FUTURE DIRECTIONS

Clinical implications

At present, GPR cannot be recommended as a stand-alone tool for predicting death in critically ill children. Evidence in the PICU is too limited, and no validated cut-off exists. However, its simplicity makes it a candidate additional marker to be studied alongside established scores. Because glucose and potassium are measured in almost every child at admission, GPR is easy to obtain, but whether it adds information beyond scores such as PRISM, PELOD-2, or PIM-3 (which is available around admission) has not yet been tested. When GPR is used, it should be interpreted together with the clinical picture, taking into account treatments that change glucose or potassium (such as insulin, dextrose, and diuretics), kidney function, the quality of the blood sample, and the child's age. Cut-offs from adult studies or from other patient groups should not be applied directly to children.

Future directions

Several steps are needed before GPR can be used in pediatric practice:

1. *Prospective, multicenter studies* in general PICU populations that include different diagnoses, such as sepsis, respiratory failure, trauma, and postoperative care, rather than a single disease.
2. *A standard way of calculating and reporting GPR,* including the units, the time of measurement (for example, the first values within 24 hours of admission), and the formula used.
3. *Age-specific cut-offs,* derived in one cohort and tested in an independent cohort, since normal values differ between neonates, infants, and older children.
4. *Direct comparison with PRISM, PELOD-2, PIM-3, and pSOFA.* In the same patients, including whether adding GPR to these scores improves discrimination and calibration.
5. *Serial measurements.* Studies should test whether changes in GPR over time, together with glucose and potassium variability, predict outcome better than a single value.
6. *Careful adjustment for confounders.* such as insulin therapy, dextrose and parenteral nutrition, diuretics, acute kidney injury, pre-existing diabetes, diabetic ketoacidosis, potassium supplementation, and hemolyzed or delayed samples.
7. *Impact studies.* that examine whether using GPR actually improves clinical decisions or patient outcomes, not only whether it predicts death.

CONCLUSIONS

The glucose-to-potassium ratio is a simple and inexpensive marker that combines two routine blood tests and may reflect the metabolic stress response in critical illness. In adults, a higher GPR has been associated with higher mortality in several conditions, although results are not consistent,

especially in sepsis. Evidence in critically ill children is very limited, with only one small study in severe traumatic brain injury identified in our search. Interpretation is further complicated by treatments that change glucose and potassium, by variability over time, and by differences in units and cut-off values between studies. At present, GPR should be seen as a promising complementary marker rather than a replacement for established scores such as PRISM, PELOD-2, and PIM-3. Prospective multicenter studies in children, with standardized calculation, age-specific cut-offs, and direct comparison with existing scores, are needed before GPR can be recommended for routine use in the PICU.

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