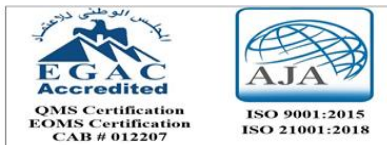




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## **Pediatric critical care services in resource-limited settings; a current state and approaches to improvement.**

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### **Abstract:**

Pediatric critical care (PCC) plays a crucial role in reducing illness and death rates globally. However, in low and middle-income countries (LMICs), PCC services are not yet well-established in many hospitals. Necessary resources, including trained healthcare staff and access to necessary medications and equipment are lacking in many pediatric intensive care units (PICUs) in LMICs. Moreover, there is a shortage of PCC training programs and certification process for healthcare providers working in PICUs and high dependency areas. Establishing a PICU in a resource-limited setting (RLSs) requires careful resource utilization. The fundamental building blocks include training healthcare staff, selecting appropriate cost-effective equipment, and having supportive leadership. If these building blocks are established in a sustainable manner, a suitable PCC service can be maintained, leading to a significant reduction in pediatric mortality and morbidity. Furthermore, there is a pressing need for conducting more researches on PCC in RLSs to provide a comprehensive view of the epidemiology and outcomes of critical illness in children. Additionally, researches should be advanced to develop appropriate guidelines for managing pediatric critical illness in RLSs and focus on low-cost critical care technology, which is vital to support critical care in LMICs. In this review, we provide an overview of the current state of PCC services in LMICs based on the current literature, and propose a contextual framework to improve these services.

**Key words:** Low-middle income countries, high –income countries, pediatric intensive care unit, staff training, cost-effective equipment.

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### **Introduction**

Pediatric critical care (PCC) services were first introduced in high-income countries (HICs) in the 1950s, and subsequently, pioneers in low-middle-income countries (LMICs) established their own services. One notable example is the opening of the first African pediatric intensive care unit (PICU) in 1969<sup>(1)</sup>. However, despite this progress, there is now a significant disparity between the quality of PCC services available in most HICs and the insufficient services available in most LMICs, as highlighted by recent studies.<sup>(2,3)</sup>

Although the mortality rate for children under the age of 5 years has decreased globally by two-thirds from the 1990 baseline to 2015, there has been only a slow decrease in the hospital case mortality rates

from the 1990s to the early 2000s. The majority of deaths are due to potentially preventable or treatable diseases such as pneumonia or diarrhea. This indicates a need for improving PCC services in order to provide a better care for the seriously-ill children<sup>(4)</sup>. LMICs face the highest burden of critical illness and pediatric mortality, while having the fewest critical care resources. Furthermore, in LMICs, children under the age of 15 make up half of the population<sup>(3)</sup>. In this article, we reviewed the relevant literature to provide an overview of the current state of PCC services in LMICs and propose a framework to improve these services.

**The current state of pediatric critical care services in resource-limited settings**

### **Mortality outcome:**

The mortality outcome of PICU in many developing countries is, in general, higher than those in developed ones. However, the mortality outcome may vary between different PICUs within developing countries according to the availability of resources.<sup>(5)</sup>

In Egypt, the mortality outcome in different PICUs was reported as follows: 14.4% in Al-Ahrar Hospital/ Zagazig;<sup>(6)</sup> 30% in Menoufia University Hospital/ Menoufia;<sup>(7)</sup> 33.1% in Cairo University Specialized Pediatric Hospitals/Cairo,<sup>(8)</sup> 37.9% in Sohag University Hospital/Sohag,<sup>(9)</sup> and 40% in South Egypt Cancer Institute/ Assuit.<sup>(10)</sup>

In other African countries, the mortality is generally high as it was reported to be 32.6% in an Ethiopian PICU<sup>(11)</sup> and 54.3% in an PICU in Malawi<sup>(2)</sup>. In other developing countries, studies performed in some units revealed mortality outcomes that may be as low as 7.9 % in the United Arab of Emirates<sup>(12)</sup> or as high as 20.9% in Iran.<sup>(13)</sup>

The primary reasons for the high mortality rates are primarily attributed to factors related to the public healthcare system, patient profile, and structure of PICUs. These factors are elaborated on in the following sections.

### **Factors related to the public health system:**

PCC services in HICs typically encompass a well-coordinated system of triage, emergency management, and PICUs that offer modern healthcare standards to the population. In contrast, LMICs face significant challenges in providing timely and equitable access to quality healthcare, emergency triage, transportation, and early identification of critical illnesses.<sup>(14)</sup>

The "three delays" model, initially formulated to explain the causes of maternal mortality, can also be applied to identify the key factors contributing to childhood mortality in LMICs, as proposed by **Thaddeus and Maine**.<sup>(15)</sup> These delays include a delay in deciding to seek medical attention, a delay in reaching the appropriate healthcare facility, and a delay in receiving quality care upon arrival at the facility. **Meligy et al**<sup>(16)</sup> noted that most of their patients belonged to low socioeconomic backgrounds and were referred to their facility in Cairo at a

late stage of their illnesses, which complicated their conditions further. According to **Ranjit and Kissoon**,<sup>(17)</sup> inadequate transportation to a suitable medical facility, lack of proper triage, and absence of organized sepsis screening and PCC support are major obstacles in reducing sepsis-related childhood mortality in resource-limited settings (RLSs).

Furthermore, rural hospitals in extremely impoverished countries, which provide about half of the medical services, often lack even the most fundamental resources such as oxygen, resuscitation equipment, and medications required for pediatric emergency care, and qualified personnel are also scarce in these areas. The COVID-19 pandemic has emphasized the significant shortage of essential resources for providing high-quality PCC services in LMICs.<sup>(17)</sup> Meanwhile, in some major cities in sub-Saharan Africa, South America, the Middle East, India, and China, urban universities and private hospitals may provide emergency and intensive care services that approach those available in HICs. This underscores the significant differences in PCC capabilities within different regions of a given LMIC.<sup>(18)</sup>

### **Patient profile:**

Several studies conducted in developing countries, including Egypt, have shown that most of patients admitted to PICUs are infants, who also have the highest age-related mortality rates.<sup>(6,8,9)</sup> This ensures the need of allocating more services to reducing the in-hospital mortality of this vulnerable population.

A significant number of children admitted to PICUs in LMICs have underlying malnutrition. A recent systematic review studied the association between under nutrition and PICU outcomes.<sup>(19)</sup> The review involved 17 studies, 11 of which were conducted in developing countries. They stated that under nutrition was significantly associated with increased risk of mortality, length of PICU stay, the use and duration of mechanical ventilation. Malnutrition can weaken a patient's immune system, making them more susceptible to infections. Hence, addressing malnutrition is crucial to improve patient outcomes and reducing their mortality.

Acute reversible medical illnesses such as infections (pneumonia, gastroenteritis and sepsis) and trauma

are the primary reasons for admission to PICUs in RLSs. <sup>(9,20,21)</sup>

In contrast, patients are occasionally admitted for postoperative care in ICUs in RLSs. PICUs, which provide postoperative care, are only available in tertiary specialized hospitals in large cities. This is because such surgical procedures require the expertise of pediatric surgery and other surgical subspecialties which are deficient in LMICs. <sup>(22)</sup> For example, in Uganda, there were only five fully trained pediatric surgeons and one pediatric anesthesiologist in the entire country in 2016. <sup>(23)</sup> This emphasizes the need for increased investment in surgical care and the training of pediatric surgeons and anesthesiologists in LICs.

### **Pediatric Intensive Care Unit Structure:**

**Dr. Paul Farmer** has outlined four essential components that should be present in the structure of PICU. <sup>(24)</sup> These components are <sup>(1)</sup> an appropriately trained healthcare staff; <sup>(2)</sup> adequate medical equipment; <sup>(3)</sup> a clean environment for patients; and <sup>(4)</sup> proper infrastructure and logistics to support the delivery of services. These components serve as a framework when establishing PCC services.

Most PCC services in low-income hospitals are provided in mixed adult-PICUs which are generally considered to be the lowest level ICU (pediatric level 2). PICUs that are established in LMICs are staffed by general pediatricians who lack specialized training as reported by many authors from the developing world. <sup>(3)</sup> According to a survey in Nepal, only one hospital had a pediatric intensivist. <sup>(21)</sup> The absence of a formal PCC training, curriculum, or certification leads to a considerable variability in understanding skills and care provided.

Nursing care also faces many challenges. Their number and training level are often insufficient to establish the recommended nurse: patient ratio of being at least 1: 3 or 4. <sup>(3)</sup> For instance, in Nigeria, with a population of 140 million people, there are just 380 nurses who have received training in ICU care. As a result, the ratio of ICU-trained nurses to patients may be as high as 1:6 in certain healthcare units located in LMICs. <sup>(25)</sup> Moreover, most available nurses do not have specialized training in providing care to critically ill patients such as adequate monitoring. <sup>(17)</sup>

In addition to the shortage of pediatric intensivists and trained nursing staff, there is a significant lack of the allied healthcare workers such as respiratory therapists, physiotherapists, clinical pharmacists, and dietitians in many resource-restricted units. <sup>(9,11,26)</sup>

In RLSs, many PICUs have a restricted number of mechanical ventilators and may lack other critical life-supporting devices, including renal replacement therapy and extracorporeal life support, as well as monitoring equipment such as invasive blood pressure monitoring and intracranial pressure monitoring devices. <sup>(11,18,26)</sup>

Inadequate space and systems in PICUs in LMICs can lead to overcrowding and disorganization, which may increase the risk of infection, make it difficult to locate essential devices, and limit healthcare staff and family access to patients. In addition, due to the deficiency of necessary infrastructure, such as pressurized gases and vacuum, more space may be needed in LMICs to accommodate equipment which is not typically necessary in HICs. For instance, in LMICs, oxygen tanks, oxygen concentrators, air compressors, and suction machines may be required in addition to monitors, intravenous pumps, renal replacement therapy and ventilators to take care for critically ill children. <sup>(3)</sup>

There is also a shortage of supporting disciplines such as laboratories and radiology services. Additionally, there may be a lack of biomedical teams available to maintain and repair equipment, leading to equipment failure and a breakdown in the unit's infrastructure. Logistic and financial limitations leading to the deficiency of medical supplies further add to the difficulty to maintain the work within the unit. <sup>(3)</sup>

Based on a recent comprehensive survey on the availability of PCC resources in LMICs, it was found that basic critical care medications were frequently absent, especially in LICs. The survey results indicated that only 65 % of ICUs in these countries consistently had all the essential human and material resources for hospital care, according to the World Health Organization (WHO) standards. <sup>(27)</sup>

## Approach to Basic Critical Care in Resource-Limited Settings

### 1- Strengthening health care system:

In LMICs, the most common causes of increased children mortality are infections many of them could have been prevented or treated at a low cost. According to the United Nations Children's Fund (UNICEF), providing universal low-cost preventive measures like breastfeeding, complementary feeding, and zinc supplementation, as well as treatment interventions such as oral rehydration therapy, antibiotics, and antimalarials could result in at least a 57% reduction in deaths among children under the age of 5.<sup>(28)</sup> It is imperative that these effective interventions are made widely available in high-mortality areas. Therefore, primary care and preventive services should be the foundation of any public health system and should receive the majority of resources.<sup>(4)</sup>

In Egypt, newborn screening program is one of the most successful national health programs.<sup>(29)</sup> First, it included congenital hypothyroidism and the phenylketonuria. Many Egyptian studies recommended expanding of the national newborn screening program to cover more inherited and treatable neonatal disorders.<sup>(29-31)</sup> In July 2021, the Ministry of Health and population has launched the President of the Republic's initiative for early detection of genetic diseases in newborns which screens for 19 genetic diseases. These diseases included many inborn errors of metabolism, congenital adrenal hyperplasia and cystic fibrosis which are prevalent in Egypt due to a high rate of consanguineous marriage.<sup>(32)</sup> This program enables early detection and management of neonates with these disorders in a presymptomatic stage. Therefore, such nationwide program would save lives and preserve the public resources.

Critical care is a crucial aspect of healthcare that is essential worldwide. When combined with efforts to identify serious illnesses within the community, facilitate early access to care, make referrals, and provide safe transport, the use of critical care services can enhance healthcare outcomes. However, limited-resource hospitals still have a deficient triage system despite WHO recommendations.<sup>(17,33)</sup> To address this issue, a simple tool called the

South African Triage Scale (SATS) has been developed, which uses clinical signs to recognize acute illness early. The implantation of SATS has led to more effective utilization of hospital resources, earlier discharge of patients, and is therefore recommended for use in LMICs.<sup>(18)</sup>

### 2- Basics of developing pediatric intensive care unit in a resource-limited settings:

#### Staff: properly trained and compensated:

The provision of effective PCC services is dependent on having a team of highly skilled and adequately remunerated medical and nursing professionals. There should be specialized training for healthcare professionals that covers knowledge, skills, and teamwork. There are a growing number of PCC fellowship programs that are aimed at training physicians in LMICs. In Egypt, a one-year PICU professional diploma program has been launched in 2022 aiming at training pediatricians to develop specialized skills for managing and improving care for seriously ill children. A similar PCC training programs, in an LMIC context, were established in Kenya, South Africa and India.<sup>(34)</sup>

In the past decade, technological progress has made it simpler to collaborate and exchange knowledge. There has been a considerable improvement in worldwide internet accessibility, and platforms have been established to enable effortless communication and interaction across the globe.<sup>(34)</sup>

With the emergence of the COVID-19 pandemic, numerous medical education centers have shifted to online learning for a wide range of topics, that include video conferencing.<sup>(35)</sup> and collaborative online training between global health partners in disparate geographical locations.<sup>(36)</sup> OPEN Pediatrics, created by Boston Children's Hospital, (available at: [www.openpediatrics.org](http://www.openpediatrics.org)), is a prime illustration of a well-established web-based platform for exchanging clinical education. This website provides access to peer-reviewed material, such as courses, expert lectures and illustrations, interactive device simulators, protocols, and medical calculators.

#### Stuff: Appropriate medical equipment:

Implementing a step-by-step process for introducing equipment can be an effective strategy for



establishing sustainable PCC services in LMICs and can help prevent the healthcare system from becoming overwhelmed. It is not necessary for the services to be expensive or heavily relying on high-end technology.<sup>(33)</sup> Moreover, it is crucial to take into account the availability of equipment in the LMIC or the region when making purchases, to ensure that it can be easily maintained and locally repaired.<sup>(3)</sup>

Respiratory support is critical in pediatric care, and non-invasive positive pressure ventilation, such as bubble continuous positive airway pressure (bCPAP), is considered a safer, more cost-effective, and sustainable option compared to ventilators. Non-invasive ventilation is preferred due to factors such as the conservation of oxygen, reduced need for sedation, lower costs, and less monitoring requirements.<sup>(3)</sup> In Ghana, simple nurse-initiated bCPAP protocols have been safely implemented for children up to the age of 5 years in non-tertiary care hospitals where there is a shortage of invasive mechanical ventilators. This has resulted in significantly a lower mortality for children receiving bCPAP.<sup>(37)</sup>

### **Space: A clean environment for treating patients:**

Caring for seriously ill patients requires more physical space compared to non-seriously ill patients, mainly due to the need for equipment and a higher number of medical staff per patient. Overcrowding in care areas can increase the risk of infection. Therefore, it is crucial to strengthen the infrastructure, including providing pressurized gases and vacuum, to avoid the need for additional equipment and ensure adequate space for patient care.<sup>(3)</sup>

### **Systems: The infrastructure and logistics for providing the services:**

The success of developing PCC services in LMICs relies on the support from local authorities, including both within the organization as well as from different levels of government. This support is crucial in developing and retaining trained medical staff. In addition, a biomedical team should be

available to provide reliable equipment replacement and repair services.<sup>(3)</sup>

### **Other important considerations:**

Establishing clear patient selection criteria for admission and discharge for every PICU is important to improve outcomes and ensure judicious use of resources.<sup>(38)</sup> For instance, the Red Cross War Memorial Hospital in South Africa published patient exclusion criteria for offering PCC to ensure fair and equitable utilization of scarce resources. Some of these exclusion criteria included children who were brain dead, children with underlying lethal conditions, such as burns occupying more than 60% of their body surface area; children with chronic renal failure for whom long-term dialysis is not available; children with lethal chromosomal abnormalities; children with malignancies unresponsive to treatment; or inoperable cardiac lesions<sup>(39)</sup>. Furthermore, in the development of PICUs in LMICs, it is crucial to establish<sup>(1)</sup> infection control strategies,<sup>(2)</sup> a sustainable supply of consumable items and medications,<sup>(3)</sup> laboratory and radiology services, and<sup>(4)</sup> data collection systems to record PICU outcomes and complications.<sup>(38)</sup>

Electronic medical records.<sup>(36)</sup> are becoming increasingly essential in critical care, especially because the prevalence of multidisciplinary, medically complex, and chronic diseases rises. In addition to well-known benefits, such as the ability to monitor labs, images, and other patients' data over time, there are more advantages, including enabling telemedicine, tele-radiology, and research.<sup>(34)</sup>

The last point is assessing the quality of service provided by PICUs in LMICs which is crucial, and one way to do this is by using quality indicators (QIs). These indicators can be evaluated using the nationally or internationally accepted benchmarks to determine the degree to which the provided health service matches the desired outcomes and identify areas for improvement.<sup>(40)</sup> Some common QIs used in PICUs include the standardized mortality ratio, length of stay, rates of ventilator-associated pneumonia, accidental extubation rate, and others.<sup>(40-42)</sup>

### ***Importance of conducting critical care research in resource-limited settings***

Although most of PCC researches are conducted in HICs, research findings in these countries may not

directly improve outcomes in RLSs. However, many recent advancements in pediatric resuscitation and PCC interventions are achieved from researches that were conducted in RLSs such as those concerning with severe sepsis, including fluid management,<sup>(33)</sup> early norepinephrine in patients with vasodilatory septic shock,<sup>(43)</sup> and the increased risk of dopamine (vs. epinephrine) as a first-line vasoactive agent in fluid refractory septic shock.<sup>(44)</sup> Furthermore, researches conducted in LMICs have demonstrated the It is important to evaluate CC practices in RLSs to ensure similar outcomes as those observed in HICs. For example, while the use of intraosseous needles in pediatric resuscitation is widely accepted in HICs, it is crucial to evaluate this practice in RLSs. A study conducted by **El-Nawawy et al**<sup>(45)</sup> in Egypt showed that the use of intraosseous lines resulted in a significantly shorter time to vascular access and reduced mortality in children with sepsis, compared to the use of intravenous catheters. Such research conducted in a LMIC helps to validate these practices and promote their acceptance in all settings.

As survival rates from pediatric serious illness continue to increase, it has become apparent that post-PICU sequelae and late mortality are a concern, highlighting the need for services to support continued recovery from critical illness.<sup>(46)</sup> For instance, one Egyptian study found increased psychiatric morbidity in PICU survivors.<sup>(47)</sup> Another study severely malnourished Bangladeshi children initially treated in the PICU for severe pneumonia had a post-discharge mortality rate of up to 8.6% within 3 months.<sup>(48)</sup>

More important is the researches that evaluate the usefulness of cost-effective technologies in RLSs. For example, many studies conducted in resource-restricted PICUs have proved the efficacy of bCPAP in respiratory support in infants and young children.<sup>(37,49,50)</sup> However, these studies were performed on individual units and multicenter studies are still needed as they more reliable to assess such interventions.

Other types of researches focus establishing services that strengthen the public health system. Thus, these services can reduce the burden of critical illness among children. A good example of

such researches is an Egyptian study published in 2016 which represented the first Egyptian newborn screening pilot study.<sup>(29)</sup> This study screened dried blood spots of 25,276 healthy newborns from three governorates in Upper, Middle, and Lower Egypt using tandem mass spectrometry. Based on the results of this study, 13 cases were identified and then confirmed to have one of inherited metabolic disorders. Hence, this study highlighted the importance of using tandem mass spectrometry in newborn screening programs for early detection and management of the most prevalent inborn errors of metabolism in Egypt. This study and other relevant studies were adopted by healthcare policy makers and a nationwide initiative for an expanded newborn screening program was launched recently in Egypt as mentioned before.

### Research perspectives

The research agenda should prioritize increasing evidence regarding critical illness epidemiology and outcomes in RLSs. Simple severity of illness scores adapted and validated for RLSs can improve patient triage and clinical research. There should be efforts should to generate critical care guidelines for common diseases in RLSs (e.g., sepsis). Further researches should focus to track and reduce the morbidity after PICU discharge in RLSs. Moreover, research in low-cost technology is important as cost-effective solutions are essential to address the resource constraints in these settings. Finally, researches should be conducted on national basis to evaluate the effectiveness of policies that improve the health care system with the best utilization of the available resources.

### Conclusion

Although PCC services are vital in improving outcome for critically ill children, they face many challenges in both human and physical resources in RLSs. To establish and sustain PCC services in LMICs, it is important to start with the basic building blocks. These include training healthcare staff in the skills and knowledge needed to provide PCC, selecting low cost but proper equipment, and having supportive stewardship. Finally, advancing researches in LMICs can impact the delivery of PCC.

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**Authors' contribution:**

MMM & RGA: conceptualized the idea, reviewed the literature, and wrote the manuscript, MAMB & RAM: critically reviewed the article for important intellectual content. All authors approved the final version of the manuscript.

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