

WHAT'S NEW IN INTENSIVE CARE



What's new in PICU in resource limited settings?

Andrew C. Argent^{1,2*}, Mohammad J. Chisti^{3,4} and Suchitra Ranjit⁵

© 2017 Springer-Verlag GmbH Germany and ESICM

It is in the richer countries of the world that critically ill children are most likely to receive care in an (paediatric) intensive care unit [(P)ICU], while most of the children in the world live in low and middle income countries (LMICs) [1]. Recently there has been substantial improvement in mortality among children in many of these LMICs, with an increased focus on the care of critically ill children. However, extracting optimal value from critical care treatment in LMICs depends on a deep understanding of the resources required to provide incremental levels of care to critically ill children, as well as a focus on the interventions that will make the most difference.

While there is no setting in the world which is not “resource limited”, the resources available for health care may differ by 100-fold across regions of the world, and even tenfold across LMICs (Table 1). In many countries there are neither funds nor trained personnel to provide critical care based on the models of Europe or the USA. In addition, disease profiles in LMICs may be profoundly different to those found in the richer countries; as such, the assumption that approaches used in rich countries will work in LMICs may be wrong.

Strategies which are new and innovative in LMICs range from organizational aspects through to identification and affordable management of common conditions (particularly those with a significant contribution to mortality) and to the identification of ways to implement change. The emphasis is often not on the “ideal” but on the pragmatic.

In many LMICs, emergency care, including triage and intensive care, is a weak link in healthcare systems. Emergency and triage training, transport training, simplified protocols and treatment algorithms have all resulted in reduced morbidity and mortality of critically ill children. Thus, increasing the focus on the pathways and delivery processes of critical care may be essential [2].

Sepsis is an important cause of mortality and severe morbidity in LMICs. Fluid resuscitation is regarded as fundamental to the management of severe sepsis. A study in Bangladesh recently reported that the lack of response to fluid resuscitation was associated with high mortality in children with severe sepsis treated in a Bangladesh PICU [3]. In this context, the finding of the FEAST study [4], namely that fluid bolus is associated with increased mortality in children with severe febrile illness and impaired perfusion, has major implications on the treatment of seriously ill children. This study has stimulated review of fluid management in severe sepsis and renewed focus on the pathophysiology of severe sepsis. Ranjit et al. recently used echocardiography to study patients with shock, and the results have provided significant insights into the complexity of the haemodynamics of severe sepsis [5] and the beneficial role of early norepinephrine [6] in patients with vasodilatory septic shock. A high-quality (single-centre) Brazilian randomized controlled trial (RCT) found that dopamine (vs. epinephrine) as a first-line vasoactive agent in fluid refractory septic shock was associated with an increased risk of death and healthcare-associated infection [7]. These results from developing countries could lead to a rethinking of the strategy that involves using dopamine as the first-line vasoactive in paediatric septic shock.

Recently, the combination of severe malnutrition, sepsis and pneumonia with fluid resuscitation in particular has

*Correspondence: Andrew.Argent@uct.ac.za

¹ School of Child and Adolescent Health, University of Cape Town, Cape Town, South Africa

Full author information is available at the end of the article

Table 1 Healthcare resources across the world by region and income category

Region/income category	Health expenditure				Healthcare workers	
	Public expenditure ^a	Out-of-pocket expenditure ^b	External resources ^c	Per capita per annum (\$)	Physicians (per 1000 people)	Nurses and midwives (per 1000 people)
Worldwide	60.1	18.2	0.2	1060	1.5	3.3
By geographical zone						
Europe & Central Asia	75.5	17	–	2419	3.4	7.5
Latin America & Caribbean	51.2	31.7	0.5	714	2	4.2
Middle East & North Africa	60.7	31.1	0.8	433	1.6	2.5
North America	49.6	11.2	–	8990	2.4	9.8
South Asia	31.2	61.5	2.3	67	0.7	1.4
Sub-Saharan Africa	42.6	34.5	11.2	98	0.2	1.2
By income zone						
Low income	42.4	37.2	33.2	37	0.1	–
Lower middle income	36.4	55.7	3.3	90	0.8	1.7
Upper middle income	54.9	32.4	0.3	514	2	3
High income	62.3	13.3	–	5251	2.9	8.6

Data in this table (modified from the World Bank database—World Development Indicators: Health systems) on total expenditure on health (not including sanitation and housing) are for the year 2014 and are presented as per capita spending per annum. Data on healthcare workers are for the period 2008–2014. <http://wdi.worldbank.org/table/2.12>, <http://data.worldbank.org/summary-terms-of-use>, <http://web.worldbank.org/WBSITE/EXTERNAL/0,contentMDK:22547097~pagePK:50016803~piPK:50016805~theSitePK:13,00.html>, <http://web.worldbank.org/WBSITE/EXTERNAL/0,contentMDK:20130471~menuPK:1>

^a Public expenditure is shown as a percentage of the total expenditure on healthcare i.e. as the percentage of total healthcare expenditure that is provided by the government

^b Out-of-pocket expenditure is shown as the percentage of total healthcare expenditure that has to come from the individual families seeking healthcare

^c External resources is the percentage of total healthcare expenditure that comes from sources outside of the particular country that is being evaluated (often aid money)

been associated with high mortality [8]. Preliminary data indicate that malnourished patients with shock do show some fluid responsiveness on bolus therapy—but they still suffer high mortality [9]. For the first time we are seeing real data on which to base future approaches and therapies.

Recent data on the pathogens responsible for severe sepsis in LMICs such as Indonesia, Thailand and Vietnam [10, 11] reveal that the pathogens in these countries differ from those in richer countries (and even in other LMICs such as Brazil [12])—even when only bacterial pathogens are considered [13]. There is a very high incidence of multidrug resistant bacterial infection and a high rate of nosocomial infection in neonatal and paediatric ICUs in LMICs [14]. Unfortunately while good facilities, adequate staffing and adequate laboratory services are essential to reduce nosocomial infection, they are expensive. “Saving” on these resources may actually translate into extra (and wasted costs).

With increased focus on severe sepsis has come the realization that problems may continue well after PICU

discharge. Wiens et al. [15] reviewed a group of children admitted to hospital in Uganda with infections and showed that the mortality in the first 6 months following discharge (4.9%) was nearly as high as that during the initial hospital admission. In severely malnourished Bangladeshi children initially treated in PICU for severe pneumonia, post-discharge (3 months) mortality was even higher (8.6%) [16]. Importantly, it is potentially possible to identify children at high risk before discharge and provide effective interventions to reduce mortality.

Respiratory infections cause significant morbidity and mortality, and non-invasive modes of ventilator support have been used extensively across the world. A RCT in Bangladesh [17] demonstrated that failure of respiratory support was lower with nasal continuous positive airway pressure (CPAP) and high-flow humidified oxygen (using simple, pragmatic and sustainable systems) than with “normal” low-flow oxygen. More recently, a large RCT of CPAP and conventional oxygen therapy in children with respiratory distress of any cause demonstrated potential

benefit from CPAP [18]. Unfortunately, the number needed to treat in this study was high, and it remains to be seen how this can be translated into appropriate and affordable practice.

Severe anaemia is a common problem in areas with a high prevalence of malaria, and optimization of transfusion protocols may have profound implications for children with limited access to transfusion (of variable quality). The critical care research group in Kenya has extended their work into the area of paediatric transfusion medicine [19].

The focus on severe sepsis and respiratory disease in children across the world seems appropriate. The focus on pragmatic management process may bridge the gap between resources and the management of complex disease processes. Most importantly, despite the challenges of healthcare delivery in LMICs, researchers in these areas have been producing high-quality studies that challenge many assumptions and paradigms of current paediatric critical care practice across the world.

Author details

¹ School of Child and Adolescent Health, University of Cape Town, Cape Town, South Africa. ² Paediatric Intensive Care, Red Cross War Memorial Children's Hospital, Klipfontein Road, Rondebosch, Cape Town, South Africa. ³ Clinical Research, Hospitals, Nutrition and Clinical Services Division (NCS), International Centre for Diarrhoeal Disease Research, Bangladesh (icddr), Dhaka, Bangladesh. ⁴ ICU, Dhaka Hospital, NCS, icddr, Dhaka, Bangladesh. ⁵ Pediatric Intensive Care, Apollo Children's Hospital, Chennai, India.

Compliance with ethical standards

Conflicts of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Received: 24 July 2017 Accepted: 9 August 2017

Published online: 14 September 2017

References

- Turner EL, Nielsen KR, Jamal SM, von Saint Andre-von Arnim A, Musa NL (2016) A review of pediatric critical care in resource-limited settings: a look at past, present, and future directions. *Front Pediatr* 4:5
- Hodkinson P, Argent A, Wallis L, Reid S, Perera R, Harrison S, Thompson M, English M, Maconochie I, Ward A (2016) Pathways to care for critically ill or injured children: a cohort study from first presentation to healthcare services through to admission to intensive care or death. *PLoS ONE* 11:e0145473
- Sarmin M, Ahmed T, Bardhan PK, Chisti MJ (2014) Specialist hospital study shows that septic shock and drowsiness predict mortality in children under five with diarrhoea. *Acta Paediatr* 103:e306–e311
- Maitland K, Kiguli S, Opoka RO, Engoru C, Olupot-Olupot P, Akech SO, Nyeko R, Mtove G, Reyburn H, Lang T, Brent B, Evans JA, Tibenderana JK, Crawley J, Russell EC, Levin M, Babiker AG, Gibb DM, Group FT (2011) Mortality after fluid bolus in African children with severe infection. *N Engl J Med* 364:2483–2495
- Ranjit S, Aram G, Kissoon N, Ali MK, Natraj R, Shresti S, Jayakumar I, Gandhi D (2014) Multimodal monitoring for hemodynamic categorization and management of pediatric septic shock: a pilot observational study. *Pediatr Crit Care Med* 15:e17–e26
- Ranjit S, Natraj R, Kandath SK, Kissoon N, Ramakrishnan B, Marik PE (2016) Early norepinephrine decreases fluid and ventilatory requirements in pediatric vasodilatory septic shock. *Indian J Crit Care Med* 20:561–569
- Ventura AM, Shieh HH, Bousso A, Goes PF, de Cassia FOFI, de Souza DC, Paulo RL, Chagas F, Gilio AE (2015) Double-blind prospective randomized controlled trial of dopamine versus epinephrine as first-line vasoactive drugs in pediatric septic shock. *Crit Care Med* 43:2292–2302
- Chisti MJ, Salam MA, Bardhan PK, Faruque AS, Shahid AS, Shahunja KM, Das SK, Hossain MI, Ahmed T (2015) Severe sepsis in severely malnourished young Bangladeshi children with pneumonia: a retrospective case control study. *PLoS ONE* 10:e0139966
- Obonyo N, Brent B, Olupot-Olupot P, Boele van Hensbroek M, Kuipers I, Wong S, Shiino K, Chan J, Fraser J, van Woensel JBM, Maitland K (2017) Myocardial and haemodynamic responses to two fluid regimens in African children with severe malnutrition and hypovolemic shock (AFRIM study). *Crit Care* 21:103
- Network SAIDCR (2017) Causes and outcomes of sepsis in southeast Asia: a multinational multicentre cross-sectional study. *Lancet Glob Health* 5:e157–e167
- Maltha J, Guiraud I, Kabore B, Lompo P, Ley B, Bottieau E, Van Geet C, Tinto H, Jacobs J (2014) Frequency of severe malaria and invasive bacterial infections among children admitted to a rural hospital in Burkina Faso. *PLoS ONE* 9:e89103
- de Souza DC, Shieh HH, Barreira ER, Ventura AM, Bousso A, Troster EJ (2016) Epidemiology of sepsis in children admitted to PICUs in South America. *Pediatr Crit Care Med* 17:727–734
- Larru B, Gong W, Vendetti N, Sullivan KV, Localio R, Zaoutis TE, Gerber JS (2016) Bloodstream infections in hospitalized children: epidemiology and antimicrobial susceptibilities. *Pediatr Infect Dis J* 35:507–510
- Singhi S, Ray P, Mathew JL, Jayashree M (2008) Nosocomial bloodstream infection in a pediatric intensive care unit. *Indian J Pediatr* 75:25–30
- Wiens MO, Kumbakumba E, Larson CP, Ansermino JM, Singer J, Kissoon N, Wong H, Ndamira A, Kabakyenga J, Kiwanuka J, Zhou G (2015) Postdischarge mortality in children with acute infectious diseases: derivation of postdischarge mortality prediction models. *BMJ Open* 5:e009449
- Chisti MJ, Graham SM, Duke T, Ahmed T, Faruque AS, Ashraf H, Bardhan PK, Shahid AS, Shahunja KM, Salam MA (2014) Post-discharge mortality in children with severe malnutrition and pneumonia in Bangladesh. *PLoS ONE* 9:e107663
- Chisti MJ, Salam MA, Smith JH, Ahmed T, Pietroni MA, Shahunja KM, Shahid AS, Faruque AS, Ashraf H, Bardhan PK, Sharifuzzaman Graham SM, Duke T (2015) Bubble continuous positive airway pressure for children with severe pneumonia and hypoxaemia in Bangladesh: an open, randomised controlled trial. *Lancet* 386:1057–1065
- Wilson PT, Baiden F, Brooks JC, Morris MC, Giessler K, Punguyire D, Apio G, Agyeman-Ampromfi A, Lopez-Pintado S, Sylverken J, Nyarko-Jectey K, Tagbor H, Moresky RT (2017) Continuous positive airway pressure for children with undifferentiated respiratory distress in Ghana: an open-label, cluster, crossover trial. *Lancet Glob Health* 5:e615–e623
- Olupot-Olupot P, Engoru C, Thompson J, Nteziyaremye J, Chebet M, Ssenyondo T, Dambisya CM, Okuuny V, Wokulira R, Amorut D, Ongodia P, Mpoya A, Williams TN, Uyoga S, Macharia A, Gibb DM, Walker AS, Maitland K (2014) Phase II trial of standard versus increased transfusion volume in Ugandan children with acute severe anemia. *BMC Med* 12:67