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Lactate as a predictor of mortality in Malawian children with WHO-defined pneumonia

Bharat Ramakrishna,[1] Stephen M Graham,[1 2] Ajib Phiri,[2] Limangeni Mankhambo,[2] Trevor Duke[1 3]

[1]Centre for International Child Health, University of Melbourne, Department of Paediatrics and Murdoch Children's Research Institute, Royal Children's Hospital, Melbourne, Australia
[2]Department of Paediatrics and Malawi-Liverpool-Wellcome Trust Clinical Research Programme, University of Malawi College of Medicine, Blantyre, Malawi
[3]Intensive Care Unit, Royal Children's Hospital, Melbourne, Australia

Correspondence to
Professor Trevor Duke, Centre for International Child Health, University of Melbourne, Department of Paediatrics, Royal Children's Hospital, Flemington Road, Parkville, Victoria, 3052, Australia; trevor.duke@rch.org.au

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ABSTRACT

Objectives To determine whether blood lactate measured at the time of presentation to hospital predicted outcome in children with pneumonia in Malawi, and to understand the factors associated with high blood lactate concentrations in pneumonia.

Design Analysis of data from a prospective study of children presenting to Queen Elizabeth Central Hospital, Blantyre, with WHO-defined severe or very severe pneumonia.

Results Among 233 children with pneumonia, the median serum lactate concentration was 2.7 mmol/l (IQR 1.8–4.4 mmol/l). 77 children (33%) had a lactate concentration of 2.1–4.0 mmol/l, and 72 children (31%) had a lactate concentration >4.0 mmol/l. 92% of children who died (23/25) had lactate >2.0 mmol/l at the time of admission to hospital. There were 10 deaths (13%) among 77 children who had a serum lactate concentration of 2.1–4.0 mmol/l; and 13 deaths (18%) in the 72 children who had lactate >4.0 mmol/l. The relative risk of death if the lactate level was above 2 mmol/l was 7.48 (1.72–32.6); sensitivity 0.92, specificity 0.39, positive predictive value 0.15, negative predictive value 0.98. Multivariable analysis showed that hypoxaemia, hyperlactataemia and age ≤12 months were independent risk factors for death from pneumonia.

Conclusions Used in conjunction with clinical risk factors and pulse oximetry for measuring oxygen saturation, lactate could play an important role in identifying the sickest patients with pneumonia in developing countries.

What is already known on this topic

- In developed countries blood lactate concentration is used as a biomarker of critical illness in young children.
- In developing countries blood lactate levels have been shown to be increased in severe malaria, severe anaemia and in some children with malnutrition.
- There have been no studies evaluating the role of blood lactate in pneumonia in developing countries.

What this study adds

- Blood lactate levels were elevated in Malawian children with pneumonia.
- Hypoxaemia, hyperlactataemia and young age were independent risk factors for death from pneumonia.
- Used in conjunction with clinical signs and oxygen saturation, lactate could play an important role in identifying the sickest patients with pneumonia in developing countries.

INTRODUCTION

Pneumonia causes at least 18% of all child deaths globally, in some countries up to a third.[1] Biomarkers that indicate pneumonia severity and suggest appropriate treatment or supportive care may help lower mortality. Currently the best predictor of pneumonia mortality risk is arterial oxygen saturation, measured by pulse oximetry (saturation of peripheral oxygen, SpO_2).[2] Lactate is a product of anaerobic cellular metabolism. It is used as a marker of poor tissue oxygen delivery, and cell hypoxia in high-income settings to monitor critically ill children, including those with severe infections,[3] low cardiac output[4] and acute respiratory distress syndrome.[5] In developing countries, elevated serum lactate has been shown to occur in severe malaria,[6] malnutrition[7] and anaemia,[8] but there has been no evaluation of its role in children with pneumonia.

Hypoxaemia occurs in at least 13% of children with severe or very severe pneumonia as defined by the WHO.[9] Hypoxaemia in pneumonia results primarily from ventilation–perfusion mismatching in consolidated lung. Elevated blood lactate may occur as an end result of hypoxaemic respiratory failure, or cardiovascular or cellular failure from associated sepsis.[10 11] The septic process associated with pneumonia or other co-morbidities may reduce lactate clearance by the liver.[12 13]

This study aimed to: (1) determine whether serum lactate concentration measured at the time of hospital admission predicted mortality in children with pneumonia; and (2) investigate the factors contributing to elevated lactate in pneumonia.

METHODS

We analysed data on children with WHO-defined severe or very severe pneumonia presenting to Queen Elizabeth Central Hospital (QECH), Blantyre, Malawi. The data were collected prospectively for a study of the aetiology

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Table 1 Characteristics and classification of study patients and serum lactate concentration

Characteristic	No. of cases (% of total)	Median lactate concentration (IQR)*	No. with serum lactate >2 mmol/l (%)
Total	233 (100%)	2.7 (1.8–4.4)	149 (64%)
Outcome			
Survived	208 (89.3%)	2.6 (1.8–4.3)	126 (61%)
Died	25 (10.7%)	4.2 (2.8–7.3)	23 (92%)
Age			
2–5 months	63 (27%)	3.1 (1.7–5.0)	39 (62%)
6–11 months	54 (23%)	2.4 (1.8–3.4)	35 (65%)
12–59 months	88 (38%)	3.0 (1.9–4.7)	55 (63%)
5–14 years	28 (12%)	2.7 (1.9–4.8)	20 (71%)
Gender			
Male	123 (53%)	3.0 (1.8–4.4)	81 (66%)
Female	107 (46%)	2.4 (1.7–5.0)	67 (63%)
Unknown	3 (1%)		
Pneumonia severity			
Severe	173 (74%)	2.6 (1.8–4.3)	107 (62%)
Very severe	60 (26%)	3.1 (1.9–5.9)	42 (70%)
Weight-for-age Z-score			
$Z > -2.0$	126 (54%)	3.1 (1.7–5.3)	77 (61%)
$-3.0 < Z < -2.0$	47 (20%)	2.7 (2.0–4.3)	32 (68%)
$Z < -3.0$	60 (26%)	2.4 (1.9–3.7)	40 (67%)
SpO_2 in air			
SpO_2 >90%	146 (63%)	2.4 (1.6–4.3)	84 (58%)
SpO_2 80–89%	50 (21%)	2.9 (2.0–5.3)	36 (72%)
SpO_2 <80%	37 (16%)	3.6 (2.3–6.3)	29 (78%)
Capillary refill time			
≤2 s	212 (95%)	2.6 (1.7–4.3)	131 (62%)
>2 s	12 (5%)	3.8 (2.6–6.6)	12 (100%)
Systolic blood pressure according to age (Z-score)			
$Z > -2.0$	126 (96%)	2.9 (2.0–5.3)	87 (69%)
$Z < -2.0$	5 (4%)	3.7 (2.6–4.0)	5 (100%)
Anaemia			
PCV ≥25%	200 (88%)	2.6 (1.8–4.4)	126 (63%)
PCV <25%	26 (12%)	3.0 (1.8–5.3)	16 (62%)
HIV infection status			
Positive	88 (38%)	2.9 (2.0–4.4)	60 (68%)
Negative	97 (42%)	2.6 (1.7–4.3)	55 (57%)
Unknown	48 (21%)	3.3 (1.9–5.6)	34 (71%)
Cotrimoxazole preventive therapy			
No	210 (90%)	2.7 (1.0–15.7)	133 (63%)
Yes	21 (9%)	3.1 (1.8–6.6)	15 (71%)
CXR findings by WHO criteria			
Radiograph not performed	22 (9%)	3.0 (1.8–4.0)	14 (64%)
Evidence of end-point consolidation and/or effusion	108 (46%)	3.0 (1.9–5.1)	72 (67%)
Evidence of interstitial infiltrate and/or hyperinflation	87 (37%)	2.6 (1.6–5.0)	54 (62%)
Normal radiograph	16 (7%)	2.5 (1.8–4.3)	9 (56%)
Findings of blood culture			
Negative	207 (89%)	2.6 (1.8–4.3)	127 (61%)
Positive for bacterial isolate	26 (11%)	3.4 (2.2–5.7)	22 (85%)

*In mmol/l.
CXR, chest x-ray; PCV, packed cell volume; SpO_2, saturation of peripheral oxygen.

of pneumonia, between July 2005 and November 2006.[14] Information recorded included age, gender, severity of pneumonia according to WHO criteria, chest radiography findings consistent with the WHO radiologic classification for pneumonia,[15] arterial oxygen saturation measured by pulse oximetry (SpO_2, %), weight-for-age (Z-score), capillary refill time, packed cell volume (PCV, %), HIV status, result of blood culture, result of thick blood film examination for malaria parasites, serum lactate concentration (mmol/l) and age adjusted systolic blood pressure (Z-score).[16 17] There was a standardised method of capillary blood collection for serum lactate concentration, PCV and thick blood film. A capillary sample

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from finger prick was analysed for lactate concentration using LactateProLT-1710 (ARKRAY Instruments, Kyoto, Japan).

Children were included in the current analysis if they had WHO-defined severe or very severe pneumonia, were between 2 months and 14 years of age, and if serum lactate concentration was measured at the time of admission. Children who had clinical features consistent with the WHO criteria for pneumonia but who were found to have other diagnoses that are characterised by respiratory distress were excluded from the analysis.[14 18]

We defined hypoxaemia as an arterial oxygen saturation measured by pulse oximetry of less than 90% when breathing air.[16] Hyperlactataemia was defined as serum lactate >2.0 mmol/l.[19] PCV of <25%, which corresponds approximately to a haemoglobin of 8 g/dl or lower, represented anaemia of at least moderate severity.[20] Severe malnutrition was defined as weight-for-age Z-score <−3.0.

Univariate and multivariate logistic regression was used to determine risk factors to mortality. Variables which were significant in univariate analysis were included in a multivariate analysis. Log-likelihood models were created to show relationships between lactate concentration and SpO_2 with predicted probability of death. The area under the receiver operating characteristics (ROC) curve was calculated for the best combination of predictors according to logistic regression. The association between lactate concentration and other clinical features was investigated using univariate and multivariate logistic regression. All statistical analyses were performed using STATA V.11.

The original study of pneumonia aetiology, including sampling of capillary blood to measure lactate, was approved by the University of Malawi College of Medicine Research and Ethics Committee and the Liverpool School of Tropical Medicine Research and Ethics Committee. Written informed consent was obtained from the patient's parent(s) or guardian(s).[14]

RESULTS

Population

A total of 350 children were enrolled in the pneumonia aetiology study following informed consent. Twenty-two were excluded from the analysis when other diagnoses were identified (these included asthma, malaria, cardiac disease, meningitis, severe anaemia and foreign body aspiration), and one child absconded before initial investigations and management were complete. Therefore, 327 children were included in the final pneumonia aetiology study analysis.[14] Of these children, 233 had serum lactate measured at the time of admission to hospital and were included in our current analysis. Characteristics

Table 2 Case-death rates according to clinical and laboratory features

Characteristic	Deaths/total no.	Case-death rate, % (95% CI)
Total	25/233	10.7 (7.3 to 15.4)
Blood lactate concentration		
≤2.0 mmol/l	2/84	2.4 (0.3 to 9.8)
2.1–4.0 mmol/l	10/77	13.0 (7.0 to 22.4)
>4.0 mmol/l	13/72	18.1 (10.7 to 28.6)
CXR findings		
Radiograph not performed	3/22	13.6 (3.9 to 34.2)
Evidence of end-point consolidation and/or effusion	5/108	4.6 (1.7 to 10.7)
Evidence of interstitial infiltrate and/or hyperinflation	17/87	19.5 (12.5 to 29.2)
Normal radiograph	0/16	0 (0 to 22.7)
Age		
2–5 months	14/63	22.2 (13.6 to 34.0)
6–11 months	10/54	18.5 (10.1 to 31.0)
12–59 months	1/88	1.1 (<0.1 to 6.8)
5–14 years	0/28	0 (0.0 to 14.3)
Pneumonia severity		
Severe	11/173	6.4 (3.5 to 11.1)
Very severe	14/60	23.3 (14.3 to 35.6)
SpO_2 in air		
SpO_2 ≥90%	6/146	4.1 (1.7 to 8.9)
SpO_2 <90%	19/87	21.8 (14.4 to 31.7)
Capillary refill time		
≤2 s	7/212	3.3 (1.5 to 6.8)
>2 s	5/12	41.7 (19.3 to 68.1)
Anaemia		
PCV ≥25%	19/200	9.5 (61 to 14.4)
PCV <25%	5/26	19.2 (8.1 to 38.3)
Weight-for-age Z-score		
Z >−2.0	16/126	12.7 (7.9 to 19.7)
−3.0<Z<−2.0	4/47	8.5 (2.8 to 20.5)
Z <−3.0	5/60	8.3 (3.2 to 18.5)
Blood culture		
Positive for bacterial isolate	2/26	7.7 (1.0 to 25.3)
Negative	23/207	11.1 (7.5 to 16.1)

CXR, chest x-ray; PCV, packed cell volume; SpO_2, saturation of peripheral oxygen.

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of these children were compared to those of the children with pneumonia who did not have serum lactate measured; no significant differences were found (data not shown).

Table 1 shows the patient characteristics and clinical classification in relation to serum lactate in the 233 children who made up the lactate study. The median age was 11 months (IQR 5–30 months). The majority was less than 5 years old, and 51% were infants. There were 173 (74%) cases of severe and 60 (26%) cases of very severe pneumonia.

The median serum lactate concentration was 2.7 mmol/l (IQR 1.8–4.4 mmol/l, range 0.8 to 19.7 mmol/l). Eighty-four children (36%) had a lactate concentration ≤2.0 mmol/l, 77 children (33%) had a lactate concentration of 2.1–4.0 mmol/l, and 72 children (31%) had a lactate concentration >4.0 mmol/l. The median arterial oxygen saturation measured by pulse oximetry was 92% (IQR 84–95%, range 35–100%). Eighty-seven children (37%) had hypoxaemia on admission (SpO_2 <90%).

Many children were underweight (mean weight-for-length Z-score: –1.76, SD 1.70). There were 47 (20%) children with a low-normal weight (–3.0<Z<–2.0), while 60 (26%) children were severely malnourished (Z <–3.0).

The majority of children had normal blood pressure for their age. The mean age adjusted Z-score for systolic blood pressure was 0.68 (SD 1.50). Only five children (4%) had a blood pressure more than two SD below normal (Z <–2.0). Most children had good peripheral perfusion (mean: 1.6 s, SD 0.7); only 12 children (5%) had a capillary refill time longer than 2 s. Twenty-six children (11%) were considered anaemic (mean overall PCV: 30.7%, SD 5.3). A total of 211 (91%) children had chest radiography performed; 108 (46%) of these children had evidence of consolidation and/or effusion, 87 (37%) children had evidence of interstitial infiltrate or hyperinflation, 16 (7%) children had normal radiographs and 22 (9%) children did not have chest radiography performed.

Six children (3%) had malarial parasites detected on thick blood film. None of these children had altered consciousness (Blantyre coma score: 5 out of 5); one had severe anaemia (PCV: 13%). Twenty-six children (11%) had a positive blood culture. The predominant bacteria identified on blood culture were *Streptococcus pneumoniae* (n=9), and *Salmonella typhimurium* (n=7).

Eighty-eight patients (38%) were HIV antibody positive; either known from previous testing or tested positive to HIV during the current admission. Only seven were receiving antiretroviral therapy (ART) and 21 (9%) were receiving cotrimoxazole preventive therapy at the time of admission. The remaining children were either HIV negative (42%) or their HIV status was unknown (20%).

Analysis of mortality

Among the 233 children, 25 died during their stay in hospital (case-death 10.7%). A summary of case-death characteristics is listed in table 2. Twenty-four deaths were in children under 12 months of age, the other child being 15 months of age (median age of deaths: 5 months, IQR 3–7 months). A higher proportion of children with very severe pneumonia died compared to children with severe pneumonia (case-death proportions 23.3% and 6.4%, respectively).

Ninety-two percent of children who died (23 out of 25) had hyperlactataemia (lactate >2.0 mmol/l) at the time of admission to hospital. There were 10 deaths (13%) among 77 children who had a serum lactate concentration of 2.1–4.0 mmol/l; and 13 deaths (18.1%) in the 72 children who had lactate >4.0 mmol/l (table 2). The median lactate concentration among children who died was 4.2 mmol/l (IQR 2.8–7.3, range 1.3–18.6), and the median lactate among survivors was 2.6 mmol/l (IQR 1.8–4.3).

Table 3 Results of univariate and multivariate analysis in predicting mortality

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Blood lactate concentration		
≤2.0 mmol/l	1.00	1.00
>2.0 mmol/l	7.48 (1.72 to 32.6)	4.68 (0.95 to 192.9)
Hypoxaemia		
SpO_2 ≥90%	1.00	1.00
SpO_2 <90%	6.52 (2.49 to 17.0)	2.96 (0.94 to 9.29)
Age		
>12 months	1.00	1.00
≤12 months	28.5 (3.79 to 215)	25.8 (3.13 to 213)
Pneumonia severity		
Severe	1.00	1.00
Very severe	4.48 (1.91 to 10.5)	1.56 (0.53 to 4.62)
HIV status		
Positive	1.00	1.00
Negative	0.27 (0.08 to 0.88)	0.19 (0.05 to 0.73)
Capillary refill time		
≤2 s	1.00	1.00
>2 s	7.26 (2.10 to 25.1)	2.89 (0.60 to 14.0)
Malnutrition		
Z >−2.0	1.00	
−2.0>Z>−3.0	0.64 (0.20 to 2.02)	
Z <−3.0	0.63 (0.22 to 1.80)	
CXR findings[15]		
Evidence of consolidation and/or effusion	1.00	
Evidence of interstitial infiltrate and/or hyperinflation	5.00 (1.76 to 14.2)	
Severe anaemia		
PCV ≥25%	1.00	
PCV <25%	2.27 (0.77 to 6.70)	
Blood culture		
Negative	1.00	
Positive	0.67 (0.18 to 3.01)	

CXR, chest x-ray; PCV, packed cell volume; SpO_2, saturation of peripheral oxygen. Other variables which were not associated (p>0.10) with mortality include: presence of bronchial breathing, grunting, tachypnoea (>70 bpm), central cyanosis, tachycardia (>160 bpm), fever (>38°C), poor feeding, prior use of antibiotics, chest indrawing, convulsions and wheeze.

Seventy-six per cent of children who died (19/25) had hypoxaemia at the time of hospital admission. The median SpO_2 was 83% (IQR 65–89%) among children who died and 93% (IQR 88–95%) among children who survived. On chest radiography, 5 (20%) of the children who died had evidence of consolidation and/or pleural effusion, and 17 (68%) children who died had evidence of interstitial infiltrate and/or hyperinflation; 3 (12%) children who died did not have radiographs performed on admission.

The median PCV for children who died was 31% (IQR 21–38%). In this analysis there was no significant association of anaemia with mortality (Kruskal–Wallis p=0.92).

Table 3 shows the results of univariate and multivariate logistic regression analyses. Children with hyperlactataemia, hypoxaemia, or who were aged ≤12 months were at greatest risk of dying from their pneumonia. Children who had evidence of interstitial infiltrate or hyperinflation were at a greater risk of dying compared to children with consolidation

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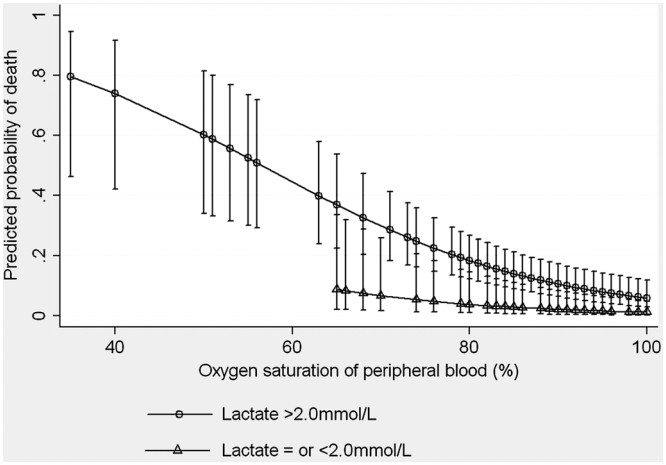


Figure 1 Log-likelihood model of saturation of peripheral oxygen (SpO_2) according to normal and elevated lactate concentrations.

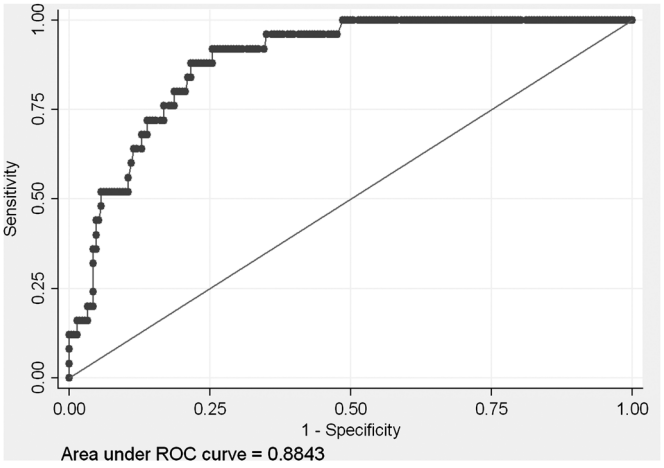


Figure 2 Receiver operating characteristics (ROC) curve of mortality, predicted by saturation of peripheral oxygen (SpO_2), age and the presence or absence of hyperlactataemia.

or effusion. The presence of hypoxaemia and young age of a child were stronger risk factors for mortality than hyperlactataemia. However, hyperlactataemia was a stronger predictor of mortality than other markers of poor perfusion status, such as capillary refill time longer than 2 s (OR 5.37, 95% CI 1.14 to 25.2 compared to OR 3.90, 95% CI 0.91 to 16.7).

Figure 1 is a log-likelihood model of lactate concentration and SpO_2 predicting mortality in these children. The model shows the probability of mortality at a given SpO_2 according to the presence or absence of hyperlactataemia. Children with hyperlactataemia were generally twice as likely to die from pneumonia compared to a child with an equivalent SpO_2 but a normal lactate level. Figure 2 is an ROC curve of age, SpO_2 and presence or absence of hyperlactataemia. These variables had an area under the ROC curve of 0.88.

Factors associated with high blood lactate

The median concentration of lactate was higher in hypoxaemic children (3.1 mmol/l, IQR 2.0–5.6 mmol/l) than in children with normal saturation (2.4 mmol, IQR 1.6–4.3 mmol/l, Kruskal–Wallis p=0.004). Higher concentrations of lactate were also found in children with capillary refill time longer than 2 s compared to children with normal refill time (median: 3.8, IQR 2.6–6.7, compared to 2.6, IQR 1.7–4.3 mmol/l, Kruskal–Wallis p=0.035). All children with capillary refill time longer than 2 s had lactate greater than 2.0 mmol/l. Systolic blood pressure was generally lower in children with hyperlactataemia (mean age adjusted Z-score 0.47 compared to 1.16 in children with normal lactate, analysis of variance (ANOVA) p=0.049). A trend was also seen in nutrition status of children. Children with hyperlactataemia tended to have poorer nutrition status compared to children with normal lactate (mean weight-for-age Z-score –1.95 compared to –1.3, ANOVA p=0.008).

DISCUSSION

This study showed that high serum lactate was a sensitive predictor of the risk of mortality in children with WHO-defined severe or very severe pneumonia; of children who died, 92% (95% CI 75% to 98%) had a lactate level above the normal range on admission. Risk factors that have been identified in previous studies (young age and hypoxaemia), were stronger predictors of mortality. A total of 126 children who had hyperlactataemia survived; thus lactate is not specific in predicting pneumonia-related mortality in the context of the treatment that could be provided at QECH.

Hypoxaemia occurs in pneumonia because of ventilation–perfusion mismatching in the lungs, right to left intrapulmonary shunts, and in very severe and late stages due to inadequate minute volume. Tissue hypoxaemia and high blood lactate can occur because of low partial pressure of arterial oxygen, or because of impaired perfusion, impaired oxygen delivery or impaired oxygen extraction from a septic state that exists in some children with bacteraemia. Lactate was a better predictor of mortality in this population than other markers of impaired cardiovascular state—prolonged capillary refill time and low systolic blood pressure. Used in conjunction with known risk factors, particularly SpO_2, lactate may contribute to clinical reasoning. A child with a given level of SpO_2 was twice as likely to die if there is also hyperlactataemia compared to a child with the same level of SpO_2 but a normal serum lactate (figure 1).

Hyperlactataemia is likely to be due to several pathophysiological mechanisms, although some may not have been identified in this study. The results suggest that hypoxaemia may lead to increased serum lactate, though the hypoxemic threshold for hyperlactataemia will differ between individuals. Sixty-five out of 87 children with hypoxaemia by definition (SpO_2 <90%) had normal lactate concentrations. No child with oxygen saturation below 67% had a normal blood lactate; this level has been described as the absolute physiological threshold for anaerobic metabolism and hyperlactataemia, in the absence of chronic cardiovascular and respiratory compensation.[11] Hyperlactataemia may be the result of poor tissue perfusion and low tissue oxygen delivery. All 12 children with capillary refill time longer 2 s had hyperlactataemia. Similarly, children with hyperlactataemia tended to have lower systolic blood pressure for their age. Similar findings are observed in children with sepsis or shock.[3 21 22] Other studies have found hyperlactataemia to be a feature of severe malnutrition, in association with hypoglycaemia and high blood pyruvate.[7] We did not record glucose or measure pyruvate concentrations, so the relationship between lactate and glucose metabolism could not be explored further.

Children with radiographic consolidation or effusion had lower risk of mortality when compared to children

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with evidence of interstitial infiltrate and hyperinflation. Radiographic findings of interstitial infiltrate, peribronchial thickening, small areas of atelectasis and hyperinflation are features of *Pneumocystis jirovecii* pneumonia (PcP),[23] as well as being consistent with viral pneumonia. There were 12 (5.1%) confirmed cases of PcP in this study group. PcP is associated with severe hypoxia and a poor outcome,[14] and it is likely that this was an underestimate of PcP cases because of the low sensitivity of the diagnostic technique used, and because few HIV-infected infants in the study were receiving cotrimoxazole preventive therapy or ART (table 1). In studies where HIV prevalence is low, radiographic evidence of consolidation and effusion has been identified as a risk factor for mortality.[24] Features in this population not found to be associated to hyperlactataemia were anaemia, bacteraemia, age and use of ART, although the numbers were small in each of these subgroups.

Not all children had chest radiography performed on admission, thus the multivariate analysis represents a subset of the study population. These results cannot be generalised beyond the population studied. Children with less severe pneumonia, symptomatic malaria, severe dehydration, meningitis, oedematous malnutrition and other common causes of hospital admission in developing countries were not included.

Further prospective studies are needed to evaluate the role of measuring serum lactate in wider hospital populations and to establish the underlying mechanisms for hyperlactataemia in pneumonia. If deemed useful in pneumonia or any of these other conditions, low cost, point-of-care serum lactate testing could better assist clinicians in their management and care of these children.

It is unclear what the response to high serum lactate should be in the clinical management of children with pneumonia. The children in Malawi with hypoxaemia received oxygen and antibiotics according to WHO treatment guidelines,[16] so it is in this context that the risk of death in those with high lactate and hypoxaemia remained higher than those with the same SpO_2 but normal lactate. It is not clear that lactate per se is injurious to organs; in fact given that the brain can metabolise lactate as well as glucose, it may be that elevated lactate has a protective effect. A randomised trial of fluid boluses in African children with febrile illness where 32% had a lactate level >5 mmol/l suggests that increased fluid is not the appropriate therapeutic response.[22] Inotropic or vasoactive drugs are rarely available in these settings. With current knowledge and therapies, perhaps the best therapy for hyperlactataemia in the setting of pneumonia is oxygen treatment at a flow sufficient to achieve a defined higher SpO_2, monitored by pulse oximetry, ensuring that there are not other signs of shock such as hypotension, and ensuring that hypoglycaemia if present is corrected. In many environments where children present with severe pneumonia, mechanical ventilation is unavailable, expensive or unsafe to implement. Simple methods of delivering continuous positive airway pressure may have a role in respiratory support. As in managing hyperlactataemia with other pathologies in other settings, there will not be one response to all situations.

CONCLUSION

Hyperlactataemia was found in many children with severe pneumonia in Malawi, and was a risk factor for death. Used in conjunction with known risk factors, young age and hypoxaemia, lactate could play a role in identifying the sickest patients. Future studies are needed to investigate the use of serum lactate as a biomarker in pneumonia and in other common conditions in developing countries. If lactate proves to augment the information currently obtainable from pulse oximetry, there is a need to evaluate whether there are any effective therapeutic responses that can be applied in settings with limited resources. The investigation of point-of-care and non-invasive serum lactate testing would be worthwhile.

Contributors SMG, AP and LM collected the original data for the study. BR and TD did the data analysis and wrote the paper. All authors contributed to the final version.

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Competing interests None.

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