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Original Research Article

Exploratory Research on the Relationship between Blood Lactate Levels and Outcomes in Children with Pneumonia

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Abstract:

Background and Objectives: Pneumonia causes at least 18% of all child deaths globally, in some countries up to a third. Biomarkers that indicate pneumonia severity and suggest appropriate treatment or supportive care may help lower mortality. The current best predictor of pneumonia mortality risk is arterial oxygen saturation, measured by pulse oximetry. Lactate is a product of anaerobic cellular metabolism. It is used as a marker of poor tissue oxygen delivery, and cell hypoxia to monitor critically ill children, patients with severe infections, low cardiac output and acute respiratory distress syndrome. There has been not much evaluation of its role in children with pneumonia. The objective is to study the association of elevated blood lactate levels in the outcome of children with pneumonia. Methods: It is an explorative study with a total of 280 cases, aged between 2 months to 14 years admitted to BMIMS Pawapuri, hospital during the study period fulfilling the inclusion criteria were included in this study. Along with the demographic data and other investigations, using aseptic precautions 2 ml of venous blood was withdrawn and sent for lactate estimation.

Conclusion: The children who died had elevated lactate concentration, hypoxia, hypotension, prolonged CFT and other signs of shock. Serum lactate measured at the time of admission, age <1 yr; hypoxia; prolonged CFT; suboptimal, feeble or low volume peripheral pulses; shock; hypotension are other strong predictors of mortality. Used in conjugation with other known risk factors like young age and hypoxemia, lactate could play a role in identifying the sick children and in their management.

Keywords: Serum Lactate; Pneumonia; Mortality.

Introduction

Acute respiratory infections can occur in any part of the respiratory system, from the middle ear to the nose to the lungs. Pneumonia is a severe form of acute lower respiratory infection that specifically affects the lungs. Most acute respiratory infections result in mild illnesses, such as the common cold. But in vulnerable children, infections that begin with mild symptoms may sometimes lead to more severe illnesses, such as pneumonia – especially when they coincide with other illnesses like diarrhea or malaria. [1] Pneumonia, defined as inflammation of the lung parenchyma, is the leading cause of death globally among children younger than age 5 yr, accounting for an estimated 1.2 million (18% total) deaths annually. The incidence of pneumonia is more than 10-fold Higher (0.29 episodes vs. 0.03 episodes), and the number of childhood-related deaths from pneumonia ≈2,000 fold higher, in Developing than in developed countries. Fifteen countries account for more than three-fourths of all pediatric deaths from pneumonia. [2]

Children with pneumonia may have a range of symptoms depending on their age and the cause of the infection. Bacterial pneumonia usually causes children to become severely ill with high fever and rapid breathing. Viral infections, however, often come on gradually and may worsen over time. Some common symptoms of pneumonia in children and infants include rapid or difficult breathing, cough, fever, chills, headaches, loss of appetite and wheezing. Children under five with severe cases of pneumonia may struggle to breathe, with their chests moving in or retractingduring inhalation (known as 'lower chest wall in drawing'). Bacterial pneumonia most often occurs when respiratory tract organisms colonize the trachea and subsequently gain access to the lungs, but pneumonia may also result from direct seeding of lung tissue after bacteremia. [2]

S. pneumonia produces local edema that aids in the

proliferation of organisms and their spread into adjacent portions of lung, often resulting in the characteristic focal lobar involvement. Group A streptococcus infection of the lower respiratory tract results in more diffuse infection with interstitial pneumonia. [4-7] *S. aureus* pneumonia manifests in confluent bronchopneumonia, which is often unilateral and characterized by the presence of extensive areas of hemorrhagic necrosis and irregular areas of cavitation of the lung parenchyma, resulting in pneumatoceles, empyema, or, at times, bronchopulmonary fistulas. [2]

Objectives

To study the association of elevated blood lactate levels in the outcome of children with pneumonia.

Material and Methods

This study was an explorative study conducted on children with WHO defined severe and very severe pneumonia in the age group of 2 months to 14 years in Pediatric Wards of Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda.

Method of Collection of Data

Random Sampling Technique without replacement and pseudo no sampling technique.

Inclusion Criteria: If they had WHO-defined severe or very severe pneumonia, Age between 2 months and 14 years.

Exclusion Criteria: With other co-morbid conditions like congenital heart disease.

Method of Study

A total of 280 cases of infants and children aged between 2 months to 14 years admitted to BMIMS Pawapuri Nalanda, Bihar. during the study period fulfilling the inclusion criteria were included in this study.

A written informed consent was obtained from the parents/guardians of all the children after fully explaining the study procedure. A detailed history, demographic data, clinical examination, severity of pneumonia according to WHO criteria, chest radiography findings consistent with pneumonia, arterial oxygen saturation measured by pulse oximetry (SpO2, %), weight-for-age (Z-score), capillary refill time, Hemoglobin (g/dL), serum lactate concentration (mg/dL) and age adjusted systolic blood pressure (Z-score). HIV status if already diagnosed was noted. Using aseptic precautions 2 ml of venous blood was withdrawn from the median cubital vein or other prominent veins in the hand without the use of tourniquet or with a tourniquet that was not released during the blood flow. It was collected in green topped heparin tube and sent to the laboratory within 1 hr of collection.

Results

280 cases were taken into this study, out of which 275 cases had serum lactate measured at the time of admission. The association of lactate and other findings are analyzed according to these 275 cases. The number of males were 169, females were 106. The median lactate concentration was 13.15mg/dL. The median lactate concentration for males was 12.44mg/dL and for females 14.54mg/dL. Majority of cases were in the age group <1yr, number being 153, whereas in 1-5 yr age group it was 103 cases and 19 were in the age group >5yr. The median lactate concentration in the age group <1yr was 18.01mg/dL which could be due to disease severity in this age group. The lactate values in this category varied from 5th percentile 7.86 to 95th percentile 34.92. 97 cases were under the very severe category of pneumonia whose median lactate concentration was 28.78mg/dL whereas for severe category it was 10.27mg/dL. 178 cases were in the severe category. 79 0f 97 cases of very severe pneumonia had elevated lactate concentration. 136 cases were in the normal weight for height category, 57 were in mild wasting category, 43 were in moderate wasting category and 39 were in severe wasting category. 23 of 39 cases in severe wasting category had elevated lactate concentration whereas it was 20 0f 43 cases in moderate wasting category. 31 of 136 cases of normal weight hot height category had elevated lactate, whereas it was 15 of 57 cases in mild wasting category. 18.22mg/dL was the median lactate value in the moderate wasting category whereas it was 23.35mg/dL in the severe wasting category, both of these values being in the higher range, which is above 19.8mg/dL. For the normal weight or height category was mild wasting category, it was within normal limits, that is 10.95 and 12.9mg/dL respectively. 125 of 275 cases had Spo2 <94%, with median lactate concentration being 26.66mg/dL, well above the normal range, 86 cases had elevated lactate concentration. 150 cases had Spo2 ≥94%, 10.34mg/dL was the median lactate concentration in this age group with only 3 cases with elevated lactate concentration. 93 of 275 cases had prolonged CFT, which is > 3sec, their median lactate concentration was 28.99mg/dL and with serum lactate concentration of 83 of these cases in the higher range. Whereas it was 182 cases in the normal CFT range, that is ≤2 sec, with median lactate concentration being 10.33mg/dL with serum lactate concentration elevated in only 9 cases. Majority of the cases, 183 of 275 cases had optimal peripheral pulse, their median lactate being 10.54mg/dL with only 7 cases had higher serum lactate values.

28 and 64 cases had suboptimal and low volume/ feeble peripheral pulses respectively. Both these categories had higher median lactate values, which is 24.67mg/dL and 29.98mg/dL respectively. 21 cases in the suboptimal group and 61 cases in low

volume/ feeble peripheral pulse group had elevated serum lactate values. 79 cases had features of shock whereas in 196 cases shock was absent, 75 cases had elevated lactate concentration in the shock group whereas it was 14 in the shock absent group. The median lactate concentration was 29.66mg/dL in the shock group and 10.84mg/dL in the group with shock absent. 54 cases had hypotension with their median lactate concentration in the higher range, which is 30.62mg/dL, 52 of these had elevated serum lactate concentration. 221 cases had normal BP whose median lactate concentration was 10.98mg/dL with only 37 cases in the elevated lactate range. 113 cases had normal Hb, whereas 161 cases had low Hb. 12.99mg/dL and 13.33mg/dL was the median lactate concentration in the normal Hb and anemia group respectively. 40 cases of normal Hb and 49 cases of anemia had elevated lactate concentration.

Table 1: Table showing the outcome.

Outcome	No. of cases
Recovered	253
Died	27
Total	280

Out of the 280 cases, 253 recovered and 27 died, with the case fatality rate being 9.6%. 26 of 27 deaths were in the age group <1yr age group.

Table 2: Serum lactate range.

Serum lactate levels	No. of cases
< 4.5 mg/dL	0
4.5- 19.8 mg/dL	186
>19.8 mg/dL	89
Not performed	5

Table 3: Relationship of mortality to peripheral pulses.

Peripheral pulses	No. of deaths
Optimal	0
Suboptimal	7
Feeble/ low volume	20

74% of deaths occurred in the category of the feeble/ low volume peripheral pulse. 31.2 was the case fatality rate in this category whereas it is 25% in the category with suboptimal peripheral pulse.

Discussion

Pneumonia causes at least 18% of all child deaths globally, in some countries up to a third. Biomarkers that indicate pneumonia severity and suggest appropriate treatment or supportive care may help lower mortality. [8, 9] The current best predictor of pneumonia mortality risk is arterial oxygen saturation, measured by pulse oximetry (saturation of peripheral oxygen, SpO2). 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, low cardiac output and acute respiratory distress syndrome. [10] In developing countries, elevated serum lactate has been shown to occur in severe malaria, malnutrition and anemia, but there has been no evaluation of its role in children with pneumonia.[10] A similar study was conducted by Bharat Ramakrishna, Stephen M Graham et al, Lactate as a predictor of mortality in Malawian children with WHO defined pneumonia, in 2006

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Table 4: Comparison of studies.

Characteristics	Our study	Malawian study
No. of cases	280	233
No. of deaths	27	25
Case fatality rate	9.6	10.7

In our study, 280 cases fulfilling inclusion criteria were taken. Serum lactate was measured in 275 of these cases at the time of admission. There were 27 deaths, all being under the age group <1yr. The case fatality rate was 9.6% which is close to the Malawian study with 10.7%. It is unclear what the response to high serum lactate should be in the clinical management of children with pneumonia. The children in our study with hypoxaemia received oxygen and antibiotics according to WHO treatment guidelines, [11] 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 SpO2 but normal lactate. It is not clear that lactate per se is injurious

to organs; in fact given that the brain can metabolize lactate as well as glucose, it may be that elevated lactate has a protective effect.

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 SpO2, 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. [11]

Conclusion

Pneumonia is one of the leading cause of mortality and morbidity in India, in our study, it had a case fatality rate of 9.64%. Serum lactate measured at the time of admission is a predictor of mortality.

Age <1 yr; hypoxia measured as Spo2 <94%; prolonged CFT; suboptimal, feeble or low volume peripheral pulses; shock; hypotension at the time of admission are other strong predictors of mortality. Very severe pneumonia children usually have serum lactate in the higher range. Radiological evidence of consolidation is a risk factor for mortality. Used in conjugation with other known risk factors like young age and hypoxemia, lactate could play a role in identifying the sick children and in their management.

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