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Original Article

Carbon dioxide tension as a reflection of different respiratory rates and chest x-ray features in children with community acquired pnemonia

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Abstract

Background Diagnosis of community-acquired pneumonia (CAP) is often made based on clinical signs and symptoms as well as laboratory and radiographic tests. Several laboratory tests including blood gas analysis (BGA) can be helpful in establishing the diagnosis. The single most direct and useful BGA is the arterial carbon dioxide tension (PCO_2). It directly reflects the adequacy of alveolar ventilation and indirectly could reflect the severity of illness.

Objective To determine the differences of clinical signs and chest X-ray features in hospitalized CAP children with low PCO_2 level and normal to high PCO_2 level.

Methods Patients with CAP in pediatric wards of Cipto Mangunkusumo Hospital who fulfilled the inclusion criteria were enrolled between July 2009 and November 2009. Patients were categorized as group with low PCO_2 level (<35 mmHg) and group with normal to high PCO_2 level (≥ 35mmHg). All data, including clinical signs, laboratory results, and radiologic features on admissions were compared between groups.

Results Thirty patients were enrolled; 20 patients belonged to low PCO_2 level group and 10 patients belonged to normal-high PCO_2 level group. Group with low PCO_2 had significantly lower respiratory rate (P = 0.047), higher blood pH level (P = 0.044), and better chest X-ray features (P = 0.010) on admission compared to group with normal to high PCO_2 level.

Conclusion Low PCO_2 level reflects better alveolar ventilation in children with CAP as described by lower respiratory rate and better chest X-ray features. **[Paediatr Indones. 2010;50:207-13]**.

Keywords: *Community-acquired pneumonia, carbon dioxide pressure, alveolar ventilation.*

Community-acquired pneumonia is one of the most important health problems affecting children over the world. Pneumonia can be broadly defined as inflammation of lung tissue due to an infectious agent that stimulates a response resulting in damage to lung tissue.[1,2] Diagnosis of community-acquired pneumonia is often made based on clinical signs and symptoms as well as laboratory and radiographic tests.[1,3,4] Tachypnea with indrawing of the respiratory muscles should alert the clinician to a presumptive diagnosis of pneumonia.[5] Chest X-Ray is an excellent tool for detecting the presence and degree of severity of pneumonias.[6] Several laboratory tests including blood gas analysis also can be helpful in establishing the diagnosis.[7]

Ventilation usually refers to movement of air in and out of the lungs. Only air that exchanges with pulmonary blood has physiologic significance.[7] In many pulmonary disorders the distribution of gas is not homogeneous, this means some alveoli are under-ventilated while others are over-ventilated.

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The mechanisms responsible for this condition are localized changes in dispensability, localized airway obstruction, and differences in expansion. Pneumonia causes localized differences in expansion and reducing the permeability per unit area of the alveolar capillary membrane. Uneven distribution of gas has important clinical and physiologic effects.[8]

The value of any blood gas analysis measurement depends on the medical personnel ability in applying it into clinical care of patient.[7] Identification of abnormality in blood gas analysis has direct clinical implication including hospitalization for more intensive observation.[9] The single most direct and useful blood gas measurement is the arterial carbon dioxide pressure (PCO_2). It directly reflects the adequacy of alveolar ventilation thus could reflect the severity of community-acquired pneumonia.[7] The main objective of this study was to determine the differences of clinical signs and chest X-ray features in hospitalized community-acquired pneumonia children with low PCO_2 level and normal to high PCO_2 level.

Methods

All children at any age with community-acquired pneumonia who admitted to pediatric ward of Cipto Mangunkusumo Hospital, in the period of July to November 2009 were enrolled to this study. Diagnosis of pneumonia was based on WHO criteria i.e. fever, tachypnea, chest wall retraction, and abnormal auscultatory findings. Tachypnea was respiratory rate greater than 60 breaths/minute in infants younger than 2 months, 50 breaths/minute in infants younger than 1 year of age and 40 breaths/minute in children older than 1 year of age. We excluded patients with other causes of respiratory distress such as cardiac failure, neurological disorders, acute lung edema cause by metabolic disorders, anatomical pulmonary defects, extrathoracal disorders that cause disturbance of respiratory effort, chronic diseases including asthma, septicemia, and patients with hospital acquired pneumonia.

Arterial blood gas analysis and complete blood count were performed on admission. All laboratory examinations were performed in Medical Laboratory Emergency Unit of Cipto Mangunkusumo Hospital. Chest X-ray was obtained in frontal projections in Radiology Installation Emergency Unit of Cipto Mangunkusumo Hospital. All images were reviewed by pediatric radiologist. The diagnosis of pneumonia was based on the presence of pneumonic changes in chest X-ray (pulmonary infiltrate, pulmonary consolidation, and other abnormalities). The level of severity indicated by number, from mild to severe (1 to 6). Complete descriptions about severity level were: 1=unilateral pericardial / parahiler infiltrate; 2=bilateral pericardial / parahiler infiltrate; 3=segmental consolidation less than one lobe; 4=consolidation in one lobe; 5=consolidation more than one lobe or less than one lobe but appears in both lungs; 6=more severe than number 5 or with other complication like pleural effusion.

Patients were categorized as group with low PCO_2 level (defined as PCO_2 level less than 35 mmHg) and group with normal to high PCO_2 level (defined as PCO_2 equal or more than 35 mmHg). Independent student's t-test was used to evaluate the difference in respiratory rate, body temperature, pH, PO_2, SaO_2, and HCO_3 level between groups. Mann Whitney-test was used to evaluate the difference of chest X-ray severity level between the groups. Results were expressed by texts, tables, and graphs. P-values lower than 0.05 were considered to be statistically significant. We didn't compare other clinical signs like chest retraction and auscultatory sign to make objective appraisal, because all patients showed those signs and difficulties.

Results

Thirty patients with community-acquired pneumonia ranging in age from 2 to 70 months (median: 8.5 months) were enrolled; 16 of them were male. The mean PCO_2 in these children was 34.1 (SD 7.9) mmHg. Twenty children were categorized as group with low PCO_2 level with mean PCO_2 29.6 (SD 3.5) mmHg and 10 children were categorized as group with normal to high PCO_2 level with mean PCO_2 42.93 (SD 6.7) mmHg. Fifteen children were suffered from malnutrition, 11 in group with low PCO_2, and 4 in the other group.

Respiratory rate and body temperature were compared between groups. We could not evaluate

clinical signs in patients equal or above 12 months old because of the small number of subjects. Patients below 12 month-old group with low PCO_2 had significantly lower respiratory rate (P= 0.047). No significant difference was found in comparison of body temperature, which means that the difference of respiratory rate was not caused by the difference of body temperature (**Table 1**).

Laboratory results were compared between groups. There was no significant difference of hemoglobin level and blood leukocyte count between groups. Examination of arterial blood gas analysis showed higher blood pH level in group with low PCO_2 (P=0.044). Other blood gas analysis parameter showed no significant difference between groups, as shown in **Table 2** and **Figure 1**.

Table 1. Comparison of respiratory rate and body temperature between groups

Clinical signs	PCO_2 < 35	PCO_2 ≥ 35	P
Equal or above 12 months old			
Number of patients	7	1	
Body temperature, mean (SD) ºC**	37.7 (0.91)	37.6	N.E
Respiratory rate, mean (SD) breath/min**	51.4 (8.77)	52.00	N.E
Below 12 month-old			
Number of patients	13	9	
Body temperature, mean (SD) ºC**	37.8 (0.90)	37.7 (0.92)	0.996
Respiratory rate, mean (SD) breath/min**	55.2 (7.94)	64.7 (13.04)	**0.047***

*Significant difference (P ≤ 0.05); NE: not evaluated; ** mean (SD)

Table 2. Comparison of laboratory results between groups

	PCO2 < 35 mean (SD)	PCO2 ≥ 35 mean (SD)	P
Complete blood count			
Hb, mean (SD) g/dL	9.82 (1.22)	10.01 (1.16)	0.691
Leukocyte, mean (SD)/µL	11,365 (7,618)	14,650 (5,690)	0.239
Blood gas analysis			
pH, mean (SD)	7.38 (0.08)	7.32 (0.05)	0.044*
PO2, mean (SD) mmHg	91.77 (27.96)	82.59 (30.52)	0.417
HCO3, mean (SD) mEq/L	20.35 (2.75)	22.31 (2.35)	0.065
Sat O2 (%)	92.58 (6.86)	90.09 (11.93)	0.472

*Significant difference (P ≤ 0.05)

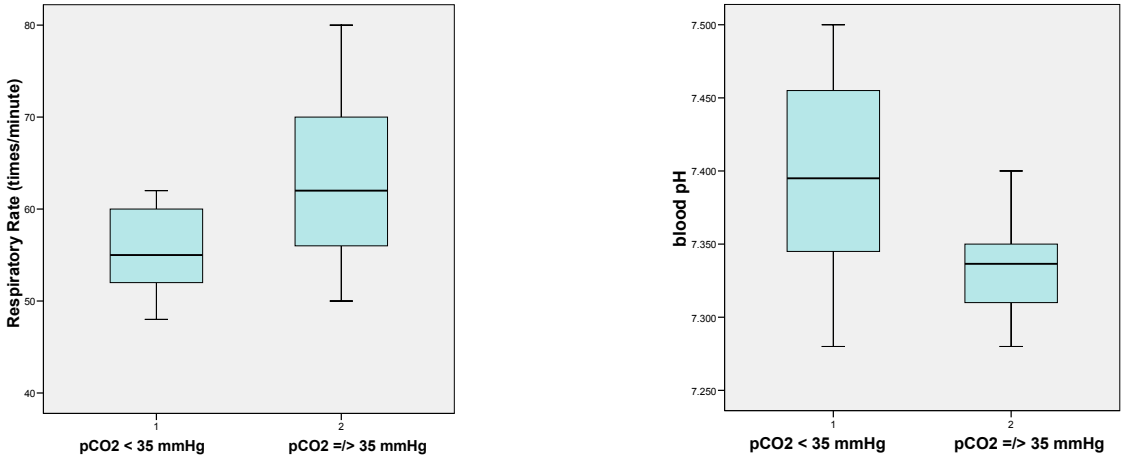

Figure 1. Box plot of (A) respiratory rate in community-acquired pneumonia patients below 12 months old with low PCO_2 and normal to high PCO_2 (B) blood pH level in community-acquired pneumonia children with low PCO_2 and normal to high PCO_2.

Table 3. Comparison of severity level based on chest X-ray between groups

	$PCO_2 < 35$	$PCO_2 \geq 35$	P
Rank 1 (n)	9	-	
Rank 2 (n)	11	9	
Rank 3 (n)	1	2	
Sum Rank	259.00	206.00	
Mean rank	12.95	20.60	**0.010***

*Significant difference ($P \leq 0.05$)

to all alveoli. The ventilation-perfusion ratio is therefore 4:5 or 0.8.[8] Since pneumonia is defined as a respiratory disease characterized by inflammation of the lung parenchyma,[10] this disorder can affect process of the gas exchange. The process can be recorded by examination of blood gas analysis.

Blood gases have been traditionally interpreted completely in relation to the acid base state. Based

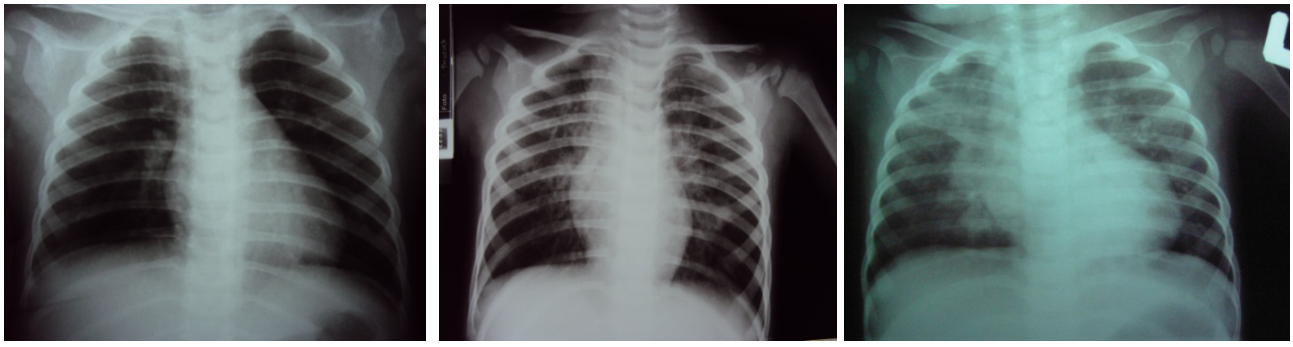

Figure 2. Example of chest X-ray features in our patients (A) Patient no. 26 categorized as rank 1 (B) Patient no. 20 categorized as rank 2. (C) Patient no. 04 categorized as rank 3.

All chest X-ray results were evaluated and classified into level of severity. Nine patients were categorized as rank 1, 18 patients were categorized as rank 2, and 3 patients were categorized as rank 3. There was no patient who fulfilled criteria for rank 4 to 6 as shown in **Figure 2**.

After comparing these images, we found significant difference of mean level of severity between groups (P=0.010). **Table 3** shows that group with low PCO2 had better chest X-ray features (less severe) compared to group with normal to high PCO2.

Discussion

Respiration is defined as the process of gas exchange between an organism and its environment. In human, this involves the exchange of gases in the lung, transport of gases in the circulatory system and gas exchange in the tissues. The primary function of the lung is gas exchange the absorption of oxygen and excretion of carbon dioxide. The volume and distribution of pulmonary capillary blood flow is as important in respiratory gas exchange as the volume and distribution of alveolar ventilation. In normal subject, pulmonary capillary blood flow is distributed

on Henderson-Hasselbalch parameters the normal range of pH was 7.35-7.45, normal range of PCO_2 was 35-45 mmHg, and normal range of HCO_3^- was 22-28 mEq/L. Arterial PCO_2 are more useful than PO_2 to reflect alveolar ventilation. There are two reasons why the arterial PO_2 may be lower than the alveolar value. One is that, even in the normal lung, some blood finds its way into the arterial system without passing through ventilation regions of the lung. This mechanism is known as shunt. Second, mismatching of ventilation and blood flow in different regions of the lung results in depression of the arterial PO_2 below the mixed alveolar value. Arterial PCO_2 is the only blood factor that participates in determining the carbon dioxide pressure gradient with alveolar air or tissue although the amount of dissolved carbon dioxide is small. In other words, the dissolved carbon dioxide determines the pressure gradient. The movement of carbon dioxide from pulmonary blood to alveolar air is dependent upon carbon dioxide pressure gradient between pulmonary blood and alveolus. Carbon dioxide passes rapidly through permeable membranes, normally the pressure are equal in alveolar air and arterial blood.[7,11] Because the PCO_2 is the direct and immediate reflection of the adequacy of alveolar ventilation, in this paper we tried to evaluate its

correlation with clinical and radiological facts. We examined the use of PCO_2 as a reflection of clinical signs and chest X-ray features in children with community acquired pneumonia.

All of our patients had clinical signs of pneumonia: fever, tachypnea, chest retractions, and crackles on chest auscultation. We didn't define the etiology of the pneumonia, but all patients were diagnosed as community-acquired pneumonia. We had two groups based on PCO_2 level. Low PCO_2 level is defined as PCO_2 less than 35 mmHg, high PCO_2 level is defined as PCO_2 more than 45 mmHg, and normal PCO_2 is between 35-45 mmHg.[12] However because of the limitation of sample size, we only categorized the patients as group with low PCO_2 level and normal to high PCO_2 level. The results of this study showed that there was significant difference in respiratory rate between groups, without significant difference in body temperature. It means that the possible cause of difference in respiratory rate was the severity of pneumonia, and not different body temperature. In group with normal to high PCO_2, tachypnea was more prominent compare to group with low PCO_2 level (**Table 1 and Figure 1A**).

Tachypnea is a useful sign for the diagnosis of childhood pneumonia. Tachypnea is more specific and more reproducible than auscultatory signs. As a clinical manifestation of hyperventilation, it is usually more sensitive and specific than crackles on auscultation. The positive predictive value of this finding is much greater in developing countries, where bacterial pneumonias are more prevalent.[1] There is an explanation why tachypnea is more prominent in group with normal to high PCO_2 level. In lung inflammation like pneumonia, which has some under ventilated areas, the excretion of CO_2 is disturbed. Retention of CO_2, can cause tachypnea as a compensation of decrease ventilated areas, and it also can cause respiratory distress and hypoxia. The width of under ventilated area has a positive correlation with severity of pneumonia. The most important factor in the control of ventilation is PCO_2 of the arterial blood.[11] In our examination patients in group with normal to high PCO_2 level, who had more prominent sign of tachypnea, had the possibility of having more severe pneumonia.

The pathologic process that caused hypoxemia and abnormal ventilation-perfusion process in pneumonia could be reflected indirectly by chest X-ray. Plain chest X-ray as part of the investigation, remains an important diagnostic tool in the evaluation of a child with pneumonia, although some pneumonia are furtive and secretive.[1,5,6] The presence of respiratory signs (e.g. tachypnea) increases the likelihood of abnormality of chest X-ray features. Patients who have pneumonia, show various patterns of chest X-ray features from mild to severe.[12] Based on this reason, we made scoring or ranking system that could describe the severity of the pneumonia (rank from 1 to 6). In our examination, consistent with the comparison of respiratory rate finding, we found that mean rank of chest x-ray severity in group with normal to high PCO_2 level was higher than group with low PCO2 level (**Table 3**).

Chest X-ray features of patient with pneumonia show the area of inflammation.[6] Clinically, it showed area with abnormality of ventilation and perfusion that can cause hypoxemia. In pneumonia, hyperventilation can decrease effect of hypoxemia.[11] Under ventilated alveoli in one area of the lung will cause failure to eliminate CO_2 normally from pulmonary capillary blood in that area. This failure can be counteracted by hyperventilation of other area since alveolar hyperventilation does increase CO_2 elimination.[8] The relation of CO_2 content to PCO_2 is nearly linear; therefore, doubling alveolar ventilation halves PCO_2 in normal ventilated alveoli.[13] Patients with more severe area of inflammation on chest X-ray, have insufficient normal alveoli, so they need more effort to eliminate CO_2. It explains why patients in group with high to normal PCO_2 level have more prominent sign of tachypnea and worse pathological process as describe by worse chest X-ray features. On the other hand, patients in group with low PCO_2 level have lower respiratory rate and better chest X-ray features.

Carbondioxide is an independent determinant of pH and is produced by cellular metabolism or by titration of HCO_3^- of metabolic acids. When alveolar ventilation is increased, it can affect a respiratory acid-base equilibrium.[14] An increase in PCO_2 will result in a decrease of pH and an increase in HCO_3^- concentration, when CO_2 is added to blood, it will produce carbonic acid and the resultant decrease of pH.[14] This may explain that we found pH level in group with normal to high PCO_2 level is lower than other group (**Table 2 and Figure 1B**).

Measurement of arterial oxygenation is important in the initial evaluation of patient with community acquired pneumonia.[9] Arterial PO_2 analysis may play a role in the diagnosis of hypoxemia in pediatric patients.[15] Arterial hypoxemia occurs whenever alveoli are under ventilated or overperfused, or the normal alveolar ventilation-perfusion ratio of 4 units of ventilation to 5 units of blood flow is not maintained.[8,16] In pneumonia, hypoxemia is a hallmark of the disease.[15] Hypoxemia in pneumonia usually due to uneven distribution of ventilation in relation to pulmonary capillary blood flow and impaired diffusion.[8,12,16] Abnormalities in the distribution of the ventilation and perfusion which is caused by increased area of under ventilated can cause intrapulmonary shunt.[8,13] Blood that reaches the systemic circulation without coming in direct contact with ventilated area of the lung is deoxygenated, and lead to arterial hypoxemia.[8,13] For this reason, PO_2 is significantly lower in patients with pneumonia.[16] In our examinations, patients in group with normal to high PCO2 level, as a group with more severe ones, were relatively more hypoxic with lower PO_2 level, but this difference was not statistically significant (**Table 2**). Oxygen saturation (SaO_2) has been used in the diagnosis of pneumonia specifically in developing countries, where a good correlation between low SaO_2 levels and pulmonary opacities on chest X-ray is observed in infants and children.[16] But in our evaluation, the SaO_2 was also not significantly different between groups (**Table 2**).

There were several limitations in our study. First, there was a limitation of sample size of the patients in this examination. Patients who were admitted to our hospital usually have complicated diagnosis, since our hospital is a referral hospital. It was difficult to find patient with simple community-acquired pneumonia without other disorders that could increase the severity of the pneumonia. Furthermore, since this is a retrospective study, s we faced problems of incomplete medical records. In the case of physical examination, findings were presumed to be absent unless specially recorded in the medical record. For that reason, we relied on objective findings such as respiratory rate and body temperature. However, despite the presence of several limitations, it is important to note that PCO_2 could be an important reflection of the severity of community-acquired pneumonia in children. Studies that criticize the correlation of pneumonia severity with arterial PO_2 and oxygen saturation (SaO_2) are frequent, but studies about its correlation with PCO_2 level are still rare. In conclusion, low PCO_2 level reflects better alveolar ventilation in children with community-acquired pneumonia as described by lower respiratory rate and better chest X-ray features.

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