IJRP.ORG
International Journal of Research Publications
ISSN: 2708-3578 (Online)

Partial Pressure of Oxygen in Stunted and Normal Growth Children and Risk Factors for Stunting by Altitude

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Abstract

Background Risk factors for stunting are not only during a child's growth period, but also during maternal period. Pregnant mothers at high altitude could influence stunted growth to the child due to low oxygen partial pressure.

Aim Observing and comparing risk factors for stunting by altitude and other contributing factors.

Methods This was a cross-sectional study conducted to patients <5 years old in Ulu Pungkut highland (700 meters above sea level) and Desa Singkuang lowland (4 – 6 meters above sea level) from March 2019. Anthropometric and oxygen partial pressure measurements were done to 38 children in the highland and 38 children in the lowland with stunted and normal growth.

Results $PaCO_2$, total CO_2 and HCO_3 values were significantly different among the research subjects residing in the lowland and highland ($p<0.0001$). There were no significant differences in oxygen partial pressure between children with stunted and normal growth.

Conclusion Subjects in highland and lowland had significant differences in $PaCO_2$, total CO_2 and HCO_3 between different altitudes in this study. However, oxygen partial pressure was not significantly different between stunted and normal growth children.

Keywords : stunting; oxygen; altitude; risk factors

1. Introduction

Stunting is a health problem in children. Stunted children have lower cognitive development than normal children, and they undergo delays in motor and language development. As a long-term effect, stunting causes low levels of productivity and learning ability. (Cruz L et al., 2017) Moreover, stunting is a public health problem which is associated with an increase risk of morbidity, impaired growth and development in children, and mortality.(Tridjaja et al., 2018)

Besides socioeconomic factors, the activities and altitudes of lands from the sea level also affect the occurrence of stunting. (Artiningrum et al., 2014). Malhotra et al. stated that hypoxic stress in highland areas is one of the environmental factors that affect impaired growth in children. The elevation of terrain has an inverse correlation with oxygen concentration in the air, where the higher the terrain is, the lower the oxygen level becomes. Partial pressure of oxygen is more significant at 3000 meters above sea level. (Ortega et al., 2006) The study done by Dang et al. at 3000 meters altitude reported higher stunting rate with higher altitudes.

Pregnant women reside in high altitudes lose birth weight of their children by an average of 100 g with an increase of 1000 meters, starting from 2000 meters altitude. Highlands cause the reduction in birth weight by restricting fetal growth in the third trimester due to the decrease in uteroplacental blood flow. Maternal adaptation to pregnancy at high altitudes is adequate in the first trimester but the ability to adapt is declining. Maternal oxygenation adapts well to hypoxia in families who have lived in the highland areas for a long period of time. (Moore et al., 2003)

Atmospheric pressure decreases up to 50% at 5500 meters above sea level and up to 30% at 8900 meters. According to Dalton's law, total atmospheric pressure is the sum of partial pressure of gasses in the air. (Peacock., 1998). Likewise, the partial pressure of oxygen decreases with atmospheric pressure. Therefore, disruptions in oxygen gas exchange may occur in pregnancy at higher altitudes and the body's oxygen needs are not fully met. As a result, babies are at risks to be delivered with low birth weight, which is one of the risk factors for stunting in children.

Indonesia is at the 5th highest rates of stunted children, where the prevalence was 30% - 39% in 2017, 30.8% in 2018 and 27.67% in 2019. This could be influenced by the geographical situation in Indonesia which varies from mountains (highlands) to valleys (lowlands). North Sumatra, which consists of coastal, lowland and highland areas, and mountains, is categorized into the region with serious stunting case where the prevalence was 28.5% and 32.93% in 2017 and 2018 respectively.This research observed the correlation between altitude and stunting in Ulu Pungkut highland at 0 – 1000 meters above sea level and Desa Singkuang, Muara Batang Gadis sub-district at 4 – 6 meters altitude. (Dinas Kesehatan Provinsi Sumatera Utara., 2019)

2. Methods

This was a cross-sectional study that assessed the difference in partial pressure of oxygen between stunted and normal growth children in Ulu Pungkut highland (700 meters above sea level, atmospheric pressure 0.9 atm or 684 mmHg) and Desa Singkuang lowland (6 – 8 meters above sea level, atmospheric pressure 0.99 atm or 752 mmHg), Mandailing Natal regency, North Sumatra on March 2019.

Research subjects were children below 5 years old with stunting or normal growth who had lived in Ulu Pungkut highland and Desa Singkuang lowland since gestational age. The exclusion criteria in this study were children who received blood transfusions in the last 3 months from March 2019, had bone growth disorder and history of familial short stature, and refused to do blood tests. The parents or guardians from the research subjects were given explanation for the research and they had signed the informed consent.

The minimum sample size was 76 research subjects, calculated by using hypothesis testing for two-sample proportions formula in cross-sectional study with 95% confidence interval (CI) and 80% power. All the research subjects were categorized into stunted and normal growth groups. Subject demographic data such as age, gender, socioeconomic status, and medical history, was taken from interviews. Anthropometric measurement (body weight and height) was performed ad plotted on WHO curve to determine growth status of the subjects. Finally, blood samples were taken (95 μL) for i-STAT blood gas analysis.

2.1 Research ethics

Parents of the research subjects were given explanations about the research and they were asked for consent to be involved in the study. This study was approved by Health Research Ethical Committee, Medical Faculty of Sumatera Utara.

2.2 Data Analysis

Collected data was processed and analyzed by using SPSS computer software system with 95% confidence interval (CI) and significance level of $P<0.05$. Multivariate analysis was carried out to determine the distribution of subject characteristics. Numerical data was presented as mean and standard deviation, while categorical data was presented in frequency and percentage. Unpaired t-test was used for normal distribution, otherwise Mann-Whitney test was carried out.

3. Results

Characteristic Data of Research Subjects

Total research sample was 76 children, in which 38 children were from Desa Singkuang lowland and 38 children were from Ulu Pungkut highland. Subject characteristic data by altitude is shown in Table 1. The majority of research subjects had good nutritional status. Drinking water source was mostly from dug wells (44,7%) and followed by unprotected wells (28.9%) in the lowland. While, the subjects in the highland mostly drank from protected springs (55.2%) and driven wells (13.1%). Parents last education levels were mostly at the primary and secondary levels in the lowland and highland respectively.

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Table 1. Subject characteristic data

Parameter	**Lowland (n = 38)**	**Highland (n = 38)**	**Total (n=76)**
Gender, n(%)			
Male	18 (47.4)	19 (50)	37 (48.7)
Female	20 (52.6)	19 (50)	39 (51.3)
Nutritional status, n(%)			
Good nutritional status	26 (68.4)	26 (68.4)	52 (68.4)
Poor nutritional status	8 (21)	6 (15.7)	14 (18.4)
Malnutrition	4 (10.5)	6 (15.7)	10 (13.2)
Drinking water source, n(%)			
Driven wells	1 (2.6)	5 (13.1)	30 (39.5)
Dug wells	17 (44.7)	8 (21)	6 (7.9)
Unprotected wells	11 (28.9)	4 (10.5)	25 (32.9)
Protected springs	9 (23.6)	21 (55.2)	15 (19.7)
Father's education level			
Illiterate	4 (10.5)	2 (5.3)	6 (7.9)
Primary school	5 (13.2)	23 (60.5)	28 (36.8)
Secondary school	24 (36.2)	12 (31.6)	36 (47.4)
High school	5 (13.2)	1 (2.6)	6 (7.9)
Mother's education level			
Illiterate	3 (7.9)	4 (10.5)	7 (9.2)
Primary school	30 (78.5)	22 (57.9)	52 (68.4)
Secondary school	5 (13.2)	10 (26.3)	15 (19.7)
High school		2 (5.3)	2 (2.6)
Age in months*, mean (SD)			33.2 (15.3)
Weight in kg*, mean (SD)			11.1 (2.5)
Height in cm*, mean (SD)			85 (9.9)
Father's height in cm**, median (min-max)			162 (155 – 178)
Mother's height in**, median (min-max)			(148 – 168)

*Numerical data with normal data distribution, i.e. mean (standard deviation)
**Numerical data with abnormal data distribution, i.e. median (min – max)

Altitude Effect on the Growth in Children

Table 2 shows the effect of altitudes towards child's growth. In lowland, 4 – 6 metes above sea level, 23 children (60.5%) had stunted growth, whereas in highland, 700 meters above sea level, 16 children (42.1%) were stunted. Statistical analysis showed no significant differences between altitudes and growth in the research subject (p=0.108).

Table 2. Children growth by altitude

Parameter		Stunting growth n (%)	Normal growth n (%)	p
Altitude	4-6 meter	23 (60.5)	15 (39.4)	0.108
	700 meters	16 (42.1)	22 (57.9)	

*Chi-square test

Partial Pressure of Oxygen with Stunting and Altitude

Partial pressure of oxygen in the research subjects at low and high altitudes was 134.3 mmHg and 131.1 mmHg respectively. Hypothesis testing between altitude and oxygen partial pressure showed no significant differences (p = 0.266). In addition, stunted growth was not significantly related to oxygen partial pressure in this research (p=0.721). Table 3 and 4 show partial pressure of oxygen data by altitude and growth respectively.

Table 3. Partial pressure of oxygen by altitude

Parameter	Altitude	n	Mean/ SD	P
PaO_2	4-6 meter	38	134.3/ 20.1	0.266
	700 meters	38	131.1/ 12.3	

*Mann-Whitney test

Table 4. Partial pressure of oxygen by growth

Parameter	Growth	n	Mean/SD	p
PaO_2	Stunting	39	132/17.5	0.721
	Normal	37	133.4/16	

*Unpaired t-test

Altitude Effect on Birth Weight and Baby Growth

The median birth weight in low altitude group was 2700 gram (range of 2200 gram – 3700 gram). Whereas, in high altitude group, the median was 2800 gram (range of 2200 gram – 3500 gram). There was no significant relationship found in this research between birth weight and altitudes (p=0.218). Similarly, there was no significant relationship between birth length and altitudes either (p=0.386). The data is presented in Table 6.

Table 5. Birth weight and length by altitude

Parameter	n	Median (Range)	P
Birth weight			
Altitude 4-6 meters	38	2700 (1500)	0.218
Altitude 700 meters	38	2800 (1300)	
Birth length			
Altitude 4-6 meters	38	48 (6)	0.386
Altitude 700 meters	38	48 (7)	

*Mann-Whitney test

Table 6 shows the relationship of birth weight and length to stunted growth. There were 7 (63.6%) stunted children in <2500 gram birth weight group and 32 stunted children (49.2%) in ≥2500 gram birth weight group. Based on birth length, 13 children (61.9%) in <48 cm group and 26 children (47.3%) in ≥48 cm group were stunted. However, the statistical analysis in this research did not find significant relationship between birth weight and length and stunting.

Table 6. Birth weight and length with stunting

Parameter		Stunted growth n (%)	Normal growth n (%)	P
Birth weight	<2500 gr	7 (63.6)	4 (36.3)	0.377
	≥2500 gr	32 (49.2)	33 (50.8)	
Birth length	<48 cm	13 (61.9)	8 (38)	0.254
	≥48 cm	26 (47.3)	29 (52.7)	

*Chi-square test

Blood Gas Analysis by Growth and Altitude

Capillary blood gas analysis was carried out to all research subjects. No significant relationships were observed in stunted and normal growth groups for pH, $PaCO_2$, total CO_2, and O_2 saturation. The data of blood gas analysis by stunted and normal growth is shown in Table 7.

Table 7. Blood gas analysis by growth

Blood gas analysis	Stunted growth (n=39)	Normal growth (n=37)	p
pH	7.54 (0.54)	7.6 (0.67)	0.157*
$PaCO_2$	12 (20.6)	11.75 (18.6)	0.19*
Total CO_2	13 (15)	13 (17)	0.66*
O_2 saturation	100 (2)	100 (3)	0.058*
HCO_3	12.9 (3.37)	12.46 (3.36)	0.58**
BE	-8.02 (3.29)	-8.21 (3.06)	0.79**
Lactate	2.53 (0.97)	2.97 (0.92)	0.05**

*Mann-Whitney test
**Unpaired t-test

On the other hand, blood gas analysis for HCO_3, $PaCO_2$ and total CO_2 levels differed significantly to altitudes with p<0.0001. The data is shown in Table 8.

Table 8. Blood gas analysis by altitude

Blood gas analysis	Altitude 4-6 meters (n=38)	Altitude 700 meters (n=38)	p
pH	7.55 (0.33)	7.6 (0.67)	0.137*
$PaCO_2$	12 (20.6)	11.75 (18.6)	<0.0001*
Total CO_2	15 (16)	12 (9)	<0.0001*
O_2 saturation	100 (2)	100 (3)	0.39*
HCO_3	14.42/ 3.34	10.95 (2.33)	<0.0001**
BE	-7 (11)	-8 (11)	0.159*
Lactate	2.57/ 1.02	2.91 (0.88)	0.128**

*Mann-Whitney test.

4. Discussion

This research was done in Ulu Pungkut highland (700 meters above sea level) and Desa Singkuang, Muara Batang Gadis sub-district lowland (4 – 6 meters above sea level), Mandailing Natal regency, North Sumatra. The proportion of stunting occurrence was at 60.5% and 42.1% in the lowland and highland respectively. Stunting cases in the highland were not only influenced by the altitude, but also by other factors, such as socioeconomic status, family income, physical activities, nutritional status and parents' education levels. These factors affect the conditions in the lowland and highland areas and influence stunting occurrence in children. (Giussani et al., 2001)

In this research, no significant relationships were observed between partial pressure of oxygen and altitudes of 4 – 6 meters and 700 meters above sea level. The human body can still well compensate inspiratory pressure at 700 meters altitude. At highlands, the body adapt by increasing ventilation due to hypoxia. This prevents the dropping of oxygen partial pressure in the alveolus with the decrease in barometric pressure. Hypoxic ventilatory response (HVR) causes the decrease in partial pressure of carbon dioxide ($PaCO_2$) in order to increase partial pressure of oxygen (PAO_2) in the alveolus. This compensates the decrease in PaO_2 in the arteries. HVR is associated with the severity of hypoxia. Significant responses occur when PaO_2 is below 60 mmHg. Besides that, alveolar hypoxia also causes pulmonary vasoconstriction to redistribute blood into the lungs, also to maximize oxygen ventilation and diffusion in the blood and alveolus. (Scheufler., 2004)

The decrease in PaO_2 in high altitudes causes reduction in oxygen content in the pulmonary capillaries. However, this may not be an issue for the people domiciled in highlands, as they have lower alveolar-arterial oxygen pressure, better diffusion capacity, and higher mean PaO_2 levels compared to people domiciled in lowlands adapting to higher altitudes.(Prasad., 2017) Adapting in higher altitudes can be defined as physiological and genetic adaptations that have taken place for years to generations in the people who have permanently resided in high altitudes. (Lumb., 2017) West stated that residents who permanently stayed in a certain altitude did not fully adapt, but their bodies have fully compensated to hypoxia in the environment. Adaptation process causes a decrease in HVR, hence reducing ventilation rate and increasing PCO_2.

Residents in high altitudes maintain PO_2 levels by increasing pulmonary diffusing capacity. This is related to the adaptations in pulmonary anatomy by increasing diffusion areas, the numbers of alveoli and associated capillaries. (Zamudio and Moore., 2000) This adaptation process is not passed down between generations, but it is occurred in children and babies residing in certain altitudes during developmental age. In humans, alveolar and saccular septation development mostly occurred after birth and the process is stimulated by hypoxia through a mechanism which is not yet clear.

The study done by Dang et al. stated than children with low birth weight had higher risk for stunting. Previous research by Moore reported that the rise in altitude increased the risk of low birth weight in children due to hypoxia during pregnancy. Birth weight and fetal growth status plays important roles in the next stages of growth in a child. Slow fetal growth occurs due to maternal-placental insufficiency; therefore, oxygen requirements are not met properly. (Shehri et al., 2005) However, this does not occur in all births at high altitudes. Differences in oxygen levels in maternal arterial and blood volumes, and remodeling of uterine vascular and vasoreactivity determine uteroplacental oxygen delivery, which play important roles in low birth weight. (Moore et al., 2003) In this research, no significant differences were observed for birth weight and length towards stunting. This finding could be caused by genetic factors that had altered uteroplacental vascular during pregnancy. Besides that, the small sample size did not represent data of birth weight and length enough. Furthermore, the data was recorded based on the memories of the parents and guardians.

There were significant differences found in $HCO_{3,}$ $PaCO_{2,}$ and total CO_2 between children in 4 – 6 meters and 700 meters altitudes. These significant differences could be explained by using the theory of Haldane Effect that explained about higher hemoglobin-CO_2 bonds in deoxygenated hemoglobin – the increase in oxygen decreases hemoglobin affinity with CO_2. The decrease in partial pressure of oxygen increases hemoglobin affinity for CO_2. (Teboul and Scheeren., 2017) A decrease in $PaCO_2$ by 5 mmHg reduces HCO_3 by 1 mEq/L. HCO_3 is an indicator for non-respiratory acid-base changes. However, it is affected by hydrolysis reaction from respiratory alkalosis or $PaCO_2$ reduction; as HCO_3 is one of the constituents in the reaction. This theory explains the different level of HCO_3 in high and low lands. (Tortora and Derrickson., 2009) This is aligned with $PaCO_2$ levels obtained in the research.

Lactic acid is produced when oxygen delivery to the tissues is reduced, resulting in anaerobic reaction – changing pyruvic acid to lactate and then diffuses it into the blood flow. (Malley., 2005) Normal lactic acid level in the body is 1.8 mmol/L, but a slight increase to up to 3 mmol/L is commonly found in several conditions, especially with stress and respiratory alkalosis involved. In this case, acidemia did not occur.

5. Conclusion

Significant relationships were found in $PaCO_2$, total CO_2 and HCO_3 levels ($p<0.0001$) among subjects in 4 – 6 meters and 700 meters altitudes. However, partial pressure of oxygen was not significantly different to stunted and normal growth children.

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