



Linear Growth of Toddlers is Affected by Infant Linear Growth, Morbidity and Micronutrient Deficiency

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Abstract

The objective of this study was to analyze the effect of birth length on linear growth of 3-year-old toddlers. We used secondary data from a longitudinal study on nutritional status of pregnant women and their offspring in Bogor Regency. The variables used were hemoglobin, serum zinc and retinol, body height, height gained, and morbidity of toddlers. A multiple logistic regression was performed to analyze the effects. The results showed that linear growth failure at birth affected the further linear growth of toddlers. Furthermore, linear growth failure of toddlers was significantly affected by the growth failure at the first year of life, morbidity rate and micronutrient deficiencies with OR= 10.5, 3.0, and 2.5 respectively. This implies the need to prevent fetal linear growth failure by improving nutritional status of pregnant women and improving micronutrient status of children to prevent the high morbidity rate that may affect the linear growth of 3-year-old toddlers.

Keywords: birth length; linear growth; micronutrient deficiency; morbidity rate; toddlers.

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1. Introduction

Linear growth failure (LGF) or height below the standard is a nutritional problem commonly found in developing countries. By using WHO growth reference standards, prevalence of stunting in under-five children reaches 38.2% in Africa, 13.5% in Latin America regions, and 27.6% in Asia. The prevalence in Thailand, Malaysia, the Philippines and Indonesia are 15.7%, 17.2%, 32.3% and 39.2%, respectively [1,2]. In Indonesia, it varies between provinces, ranging from 22.5% to 58.4%. It indicates that stunting remains a public health problem in all provinces in Indonesia, based on WHO threshold for non-public health problem (20%) [3].

According to Uauy [4], children born stunted due to fetal malnutrition not only have low height-for-age, but also may provide short- and long-term effects. In short term, stunting may increase morbidity and mortality rates, mainly due to infectious diseases such as diarrhea, measles, respiratory tract infection and malaria; thus, resulting in growth failure of the children. Stunting also has long-term effects such as decreasing intelligence level at school age, lowering the productivity in productive period, and resulting in lower earnings than the ones who are not stunted. In addition, in adulthood, stunted children are at risk of becoming overweight and having other metabolic complications, and ultimately at a higher risk of having degenerative diseases such as cardiovascular disease. Economically, short- and long-term effects of stunting may decrease average income of a country by 3.4%. Although regional and global prevalence of stunting are quite high, the determinant factors of LGF have not heretofore been obtained with certainty. Several epidemiologic studies show that suboptimal breastfeeding, supplementary feeding practice, frequency of having infectious diseases and long-term micronutrient deficiency are risk factors for LGF. Social factors such as access to health care, education, and environmental condition also play an important role in the high incidence of LGF in under-five children [5,6]. Nutritional status of the newborns, observed either from birth weight or birth length, is an important factor in the growth of infants and children. A community-based cohort study on 1-year-old toddlers in rural Malawi proved that mother with height below 150 cm, birth weight, inappropriate complementary feeding and high morbidity rate were the causal factors of stunting at 1 year of age [7]. Results of a study conducted by Schmidt and his colleagues [8] in 2002 in Bogor, West Java, showed that birth weight and length were strong predictors of nutritional status and infant linear growth until the age of 15 months. It means that normal nutritional status and adequate intake of nutrients just before and during pregnancy affect nutritional status and growth during infancy. LGF or stunting begins in utero and continues during the first two years of life, known as the first 1,000 days of life. This period is considered as a window of opportunity for intervention. Height growth pattern of under-five children in three regions (Asia, Africa, Latin America and the Caribbean) have similarities, in which there is a sharp decline in length-for-age Z-scores (LAZs) from the age of 3 months to 9 months. The decline continues until the age of 24 months although it is not as big as that period [9]. Based on the description above, this study aimed to analyze the differences in linear growth between children with growth failure and the normal ones, and to analyze the risk factors for LGF in toddlers aged 3 years.

2. Materials and Method

2.1. Design, location and time of study

The data were obtained from a longitudinal study by Center for Applied Health Technology and Clinical

Epidemiology (CAHTCE) conducted in five districts in Bogor Regency from 2011 to 2012.[10] The study was conducted in three phases. Phase 1 was conducted in 2011 on 323 mothers with gestational age of 12-14 weeks, and continued to phase 2 conducted in 2012 on infants aged 0-12 months born to pregnant women in phase 1.[11] Phase 3 was conducted in 2015, when the children in phase 2 reached the age of 3 years.

2.2. Research subjects

A total sample in phase 1 of the study was 323 pregnant women. The total sample became 262 infants in phase 2 and 190 toddlers aged 3 years in phase 3. Of that amount, there were 150 children with complete data including the length/height at age 6 months, 1 year and 3 years; consisting of 39 infants with birth LAZs ≤ -1 SD (LGF) and 111 with LAZs more than -1 SD (normal).

2.3. Data type and collection method

The dependent variable in this study was the change in linear growth of normal toddlers and the toddlers with intrauterine growth restriction. The independent variables for the changes in linear growth of 3-year-old toddlers were LAZ-based nutritional status at birth, age 6 and 12 months; hemoglobin levels; serum zinc levels; serum retinol levels; and morbidity in the last one month. Linear growth data were obtained from the measurement of body length at birth, age 6 and 12 months. The body length was measured in recumbent position by using measurement tool for body length with a degree of precision of 0.1 cm. Body height of the 3-year-old toddlers was measured in standing position by using microtoice with a degree of precision of 0.1 cm. Morbidity rates were determined by interview using questionnaires. Blood biochemical parameters collected were hemoglobin (Hb), serum zinc, and serum retinol. Hb levels in the blood were analyzed by using the cyanmethemoglobin method, serum retinol levels were measured by high pressure liquid spectroscopy (HPLC) method, and serum zinc levels were analyzed by using atomic absorption spectrophotometry (AAS) method.

2.4. Data processing and analysis

Linear growth was determined based on height-for-age Z-score (HAZ). Toddlers were defined as having LGF if their HAZs were ≤ -1 SD, and normal if more than -1 SD. Morbidity data were categorized as “often” if the frequency of sickness was ≥ 4 times/month and “seldom” if less than 4 times/month. Micronutrient-based nutritional status included Hb, serum retinol and zinc concentration. Hb level in the blood was categorized as low if it was less than 11 g/dL and normal if ≥ 11 g/dL. Serum retinol was low if it was less than 20 μ g/dL and normal if ≥ 20 μ g/dL. Meanwhile, serum zinc was categorized as low if its level was less than 0.7 mg/L and normal if ≥ 0.7 mg/L [12].

We performed univariate, bivariate, and multivariate analyses. Univariate analysis was used to analyze subjects' characteristics; changes in linear growth at birth, age 1 year and 3 years; morbidity rate; and micronutrient status. Bivariate analysis was performed to analyze the changes in linear growth and the association between the risk factors and LGF by using chi-square test. Multivariate analysis (multiple logistic regression) was used to determine the risk factor that contributes the most in growth pattern of 3-year-old toddlers.

2.5. Ethical clearance

This study was a secondary data analysis of a longitudinal study conducted by CAHTCE. Therefore, the ethical approval referred to the main study which was obtained from the Ethic Committee of National Institute of Health and Research Department (NIHRD) Number: LB.02.01/5.2/KE.233/2015. The toddlers' parents signed the informed consent as the approval of being the research subjects.

3. Results and Discussion

3.1. Subjects' characteristics

There were no significant differences found in maternal age during pregnancy, frequency of pregnancy, maternal education and number of family members between normal infants and the ones with birth-length faltering (Table 1).

Table 1: Maternal characteristics

Characteristics	LGF	Normal	p-value
Maternal age during pregnancy			
< 20 years or > 35 years	12 (30.8)	27 (24.3)	0.564
20-35 years	27 (69.2)	84 (75.7)	
Frequency of pregnancy			
> 2 times	8 (20.5)	21 (20.6)	1.000
≤ 2 times	31 (79.5)	81 (79.4)	
Maternal education			
Junior high school or lower	35 (89.7)	89 (80.2)	0.266
Senior high school or higher	4 (10.3)	22 (9.8)	
Number of family members			
> 5 people	11 (28.2)	31 (27.9)	1.000
≤ 5 people	28 (71.8)	80 (72.1)	

Table 2 showed that birth-length faltering (BLF) was more common among male infants (53.9%) than female infants (46.1%). Birth weight was directly proportional to birth length, which was seen from 29.1% of BLF infants ($p=0.005$) who had low birth weight (LBW). Birth length had a significant association with the body

length of 12-month-old infants ($p=0.038$).

Table 2: Nutritional status of children aged 0-3 years

Characteristics	Growth failure	Normal	p-value
Infant's gender			
Male	21 (53.9)	50 (45.0)	0.447
Female	18 (46.1)	61 (55.0)	
Birth weight	2835.1 $\pm$ 385.3	3347.2 $\pm$ 548.6	
< 2500 gram	7 (21.9)	2 (1.8)	0.005
$\geq$ 2500 gram	32 (82.1)	109 (98.2)	
Birth length	46.87 $\pm$ 1.19	50.04 $\pm$ 1.94	
Body length at age 6 months	64.91 $\pm$ 2.53	65.82 $\pm$ 2.46	
LGF	17 (43.6)	29 (26.1)	0.067
Normal	22 (56.4)	82 (73.9)	
Body length at age 12 months	72.19 $\pm$ 2.05	73.16 $\pm$ 2.58	
LGF	24 (61.5)	45 (40.5)	0.038
Normal	15 (38.5)	66 (59.5)	
Height at age 3 years	91.42 $\pm$ 2.89	93.06 $\pm$ 4.20	
LGF	33 (84.6)	79 (71.2)	0.148
Normal	6 (15.4)	32 (28.8)	

3.2. Linear growth patterns of children aged 0-3 years

Figure 1 showed that mean birth LAZ of LGF infants and normal infants were -1.38 ± 0.52 and 0.35 ± 1.03 , respectively. In the first three months, LAZ of LGF infants increased but declined in subsequent months. Meanwhile, it steadily declined in normal-length infants and a substantial decline occurred in the span of the third and sixth months.

However, until the age of 3 years, infants with normal length still had a higher mean HAZ (-1.63) than the ones with LGF since birth (-1.98).

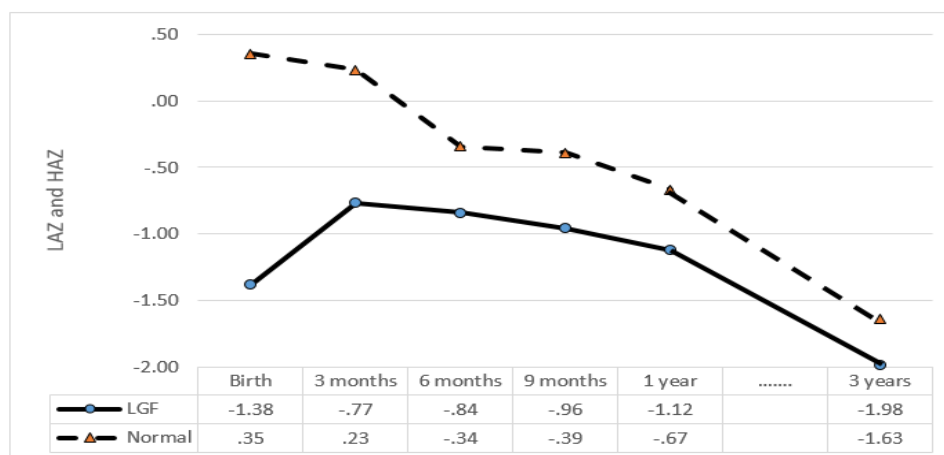


Figure 1: Mean LAZ or HAZ from birth until the age of 3 years

The results of our study showed that mean LAZ or HAZ of the newborns (-0.1) continued to decline until the age of 3 years (-1.7). Linear growth patterns in this study were consistent with the results in previous studies which indicated that stunting had started in utero and continued until the age of 2 years [13,14]. It was evident from mean LAZ of the newborns in developing countries (-0.5 SD) which continued to decline after birth and reached its lowest point (around -2.0 SD) at the age of 18-24 months. Similar results were found in cohort studies in five countries, i.e. Brazil, Guatemala, India, the Philippines, and South Africa. Mean LAZ of the newborns ranged from -0.22 in the Philippines to -1.47 in Guatemala. At the age of 2 years, there was a decline in mean LAZ ranging from -0.61 in Brazil to -3.28 in Guatemala [15].

3.3. Birth-length faltering and linear growth failure in 3-year-old toddlers

In the period of 0-12 months, there were 24 (61.5%) infants with LGF at birth who also had the same condition at the age of 12 months. On the other hand, in normal-birth-length infants group, there were 45 (40.5%) infants with LGF at the age of 12 months. Therefore, the overall relative risk (RR) was 1.518 (95% CI: 1.086-2.122; $p=0.023$). It indicated that infants with growth failure at birth had 1.5 times higher risk to remain as LGF toddlers at the age of 1 year (Figure 2). Infants with normal birth length had 1.7 times chances to have decreased nutritional status at age 3 years ($RR=1.665$; 95% CI: 1.526-2.080). Figure 2 showed that of 39 infants with BLF, only 15.4% who had normal body height at age 3 years. On the contrary, 71.2% of 111 infants with normal birth length had LGF.

The pattern of decline in HAZ resulted in increased proportion of LGF problem with age; i.e. from 26.0% at birth to 30.7% at age 6 months, 46% at age 12 months, and 74.7% at age 3 years. It indicated that LGF was difficult to overcome until the age of 3 years. Increased prevalence of stunting was also found in the study by Svefors and his colleagues in Bangladesh [16].

Linear growth in three regions (Africa, Asia, Latin America and the Caribbean) had the same pattern in which LGF began during the first month of life, faster than weight faltering which occurred at 3 months of age [9].

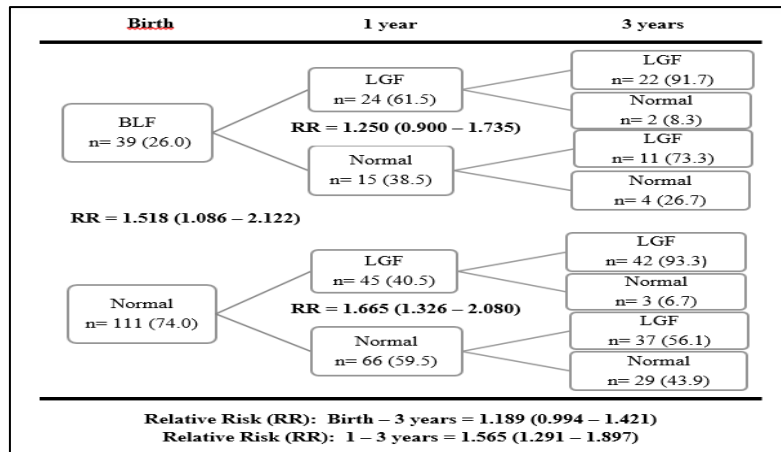


Figure 2: Linear growth of children aged 0-3 years

3.4. Risk factors for linear growth in children aged 0-3 years

At the age of 0-3 years, children's linear growth was significantly affected by length faltering that occurred from age 6 months to 1 year with OR values of 5.100 and 8.800. The high rate of morbidity in the last one month had an effect on linear growth of the 3-year-old toddlers. Toddlers who got sick more than four times in the last one month had 2.4 times higher risk of having LGF at age 3 years (OR=2.357; 95% CI: 1.098-5.059).

Table 3: Relation of birth-length, morbidity, and micronutrient status with linear growth of children aged 0-3 years

Variables	LGF n (%)	Normal n (%)	OR (95% CI)	p-value
Birth-length				
LGF (LAZ ≤ -1 SD)	33 (29.5)	6 (15.8)	2.228	0.085
Normal (LAZ > -1 SD)	79 (70.5)	32 (84.2)	(0.851-5.830)	
Length at age 6 months				
LGF (LAZ ≤ -1 SD)	42 (37.5)	4 (8.7)	5.100**	0.001
Normal (LAZ > -1 SD)	70 (62.5)	34 (89.5)	(1.690-15.389)	
Length at age 1 year				
LGF (LAZ ≤ -1 SD)	64 (57.1)	5 (7.2)	8.800**	0.000
Normal (LAZ > -1 SD)	48 (42.9)	33 (86.8)	(3.198-24.217)	
Frequency of sickness (morbidity) in the last one month				
Often (≥ 4 times)	66 (58.9)	14 (37.8)	2.357*	0.026
Seldom (< 4 times)	46 (41.1)	23 (62.2)	(1.098-5.059)	
Hb at age 3 years				
Low (< 11 g/dL)	24 (21.8)	7 (18.4)	1,236	0.654
Normal (≥ 11 g/dL)	86 (78.2)	31 (81.6)	(0.484-3.153)	
Serum zinc at age 3 years				
Low (< 0.7 mg/L)	66 (65.3)	16 (44.4)	2.357	0.029
Normal (≥ 0.7 mg/L)	35 (34.7)	20 (55.6)	(1.086-5.115)	
Serum retinol at age 3 years				
Low (< 20 µg/dL)	12 (11.3)	1 (2.6)	4.723	0.074
Normal (≥ 20 µg/dL)	94 (88.7)	37 (97.4)	(0.593-37.626)	

*) p value ≤ 0.05; **) p-value ≤ 0.01

Table 4: Risk factors for linear growth failure in children aged 1-3 years

Risk factors	OR (95% CI)	p-value
Linear growth failure at age 1 year (HAZ <-1 SD)	10.511 (3.527-31.325)**	0.000
Often get sick in the last one month (≥ 4 times)	2.522 (1.033-6.159)*	0.042
Zinc deficiency (serum zinc level < 0.7 mg/L)	3.031 (1.222-7.515)*	0.017
Vitamin A deficiency (retinol serum < 20 μ g/dL)	7.455 (0.802-69.254)	0.077

*) p-value ≤ 0.05 ; **) p-value ≤ 0.01

Data analysis on risk factors for LGF of children aged 0-3 years (Table 4) showed that linear growth at age 1 year was a risk factor for LGF in 3-year-old toddlers with OR value of 10.511 (95% CI: 3.527-31.325; $p=0.000$). Other factors that might increase the risk of LGF in 3-year-old toddlers were zinc and vitamin A deficiencies, as well as how often the toddlers got sick in the last one month with OR values of 2.522, 7.455 and 3.031, respectively. From the above equations, we got R^2 value of 0.349 ($p=0.000$). It indicated that 34.9% of LGF that occurred among the 3-year-old toddlers were determined by the linear growth at age 1 year, the high levels of zinc and vitamin A, as well as how often they got sick in the last one month. Growth is a continuous process occurring in four phases of life; i.e. fetus, infant, child and puberty. Each phase is managed by different regulatory mechanisms and affected by endogenous factors (biological, genetic and determinant of ethnic) and exogenous factors (nutrition, culture, environment and social conditions). These four phases of growth are inextricably linked to one another. If growth failure occurs in one phase, it will affect the next growth phase if it is not balanced with catch-up growth [17]. The theory above is in line with this study, in which the linear growth of newborns until they are at age 1 year affects the length faltering which occurred in 3-year-old toddlers. Infants with LGF at age 6 months were 22.3 times at higher risk of having LGF at age 1 year. Meanwhile, the linear growth of 3-year-old toddlers was significantly affected by length faltering that occurred at age 1 year with an OR value of 8.800. High morbidity of infectious diseases might decrease the nutritional status of 3-year-old toddlers. It was associated with micronutrient deficiencies, especially low Hb, serum retinol and serum zinc levels. Previous study proved that serum retinol levels in children with upper respiratory tract infection were lower than the healthy ones [18]. Similar results were obtained from another study in which iron, vitamin A and serum zinc were significantly lower in stunted children than the normal ones [19]. It indicates that vitamin A, zinc, and iron play an important role in linear growth. Zinc and vitamin A play a role in the immune system; thus, contributes to morbidity and growth failure. Zinc also plays a role in some of growth process through formation and secretion of growth hormones, activation of insulin-like growth factors (IGFs) and bone formation [19,20]. Limitations of this study were (1) the incomplete data, and lost to follow-up samples that may affect significance and power of data analysis. From 262 samples at the baseline only 150 children have complete data and can be analyzed; (2) no data collection of environmental factors such as home sanitation, use of clean water and smoking habits that can cause a high morbidity; (3) no analysis of food consumption data of

children due to the consumption data on the previous study were collected by 24 hours food recall method carried out once every month, so it does not reflect the daily intake.

4. Conclusion and Recommendation

This study indicated that length faltering at birth, age 6 months, an age 1 year had a significant effect on linear growth of 3-year-old toddlers. It is difficult for children with BLF to have a normal body length. On the contrary, children with normal birth length have a great chance to have LGF at age 3 years. LGF at age 0-1 years, morbidity, and micronutrient deficiencies are three factors which affect the linear growth of 3-year-old toddlers. Fetal LGF should be prevented by improving the nutritional status of pregnant women and improving micronutrient status of the toddlers to prevent the high morbidity rates and LGF in 3-year-old toddlers.

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References

- [1] WHO. Nutrition Landscape Information System (NLIS) Country Profile Indicators: Interpretation Guide. Switzerland: World Health Organization, 2010.
- [2] WHO. World Health Statistics 2013. Geneva: World Health Organization, 2013
- [3] Balitbangkes. Pokok-Pokok Hasil Riskesdas Indonesia 2013. Jakarta: Kementerian Kesehatan Republik Indonesia, 2013.
- [4] R. Uauy, J. Kain and C. Corvalan. "How can the developmental origins of health and disease (dohad) hypothesis contribute to improving health in developing countries?" *American Journal of Clinical Nutrition*, vol. 94 (6 Suppl), pp. 1759s-1764s, Dec. 2011.
- [5] Hermina and S. Prihatini. "Gambaran keragaman makanan dan sumbangannnya terhadap konsumsi energi protein pada anak balita pendek (stunting) di Indonesia". *Bulletin Penelitian Kesehatan*, vol. 39(2), pp. 62-73, 2011.
- [6] M.N. Hairunis, N. Rohmawati and L.Y. Ratnawati. "Determinan kejadian stunting pada anak balita di wilayah kerja Puskesmas Soromandi Kabupaten Bima Nusa Tenggara Barat". *E-Jurnal Pustaka Kesehatan*, vol. 4(2), pp. 323-329, 2016.
- [7] M. Espo, T. Kulmala, K. Maleta, T. Cullinan, M. Salin and P. Ashorn. "Determinants of linear growth and predictors of severe stunting during infancy in Rural Malawi". *Acta Paediatric*, vol. 91, pp. 1364-1370, 2002.
- [8] M.K. Schmidt, S. Muslimatun, C.E. West, W. Schultink, R. Gross and J.G. Hautvast. "Nutritional status and linear growth of Indonesian infants in West Java are determined more by prenatal environment than by postnatal factors". *Journal Nutrition*, vol. 132, pp. 2202-2207, Aug. 2002.
- [9] R. Shrimpton, C.G. Victora, M. Onis, R.C. Lima, M. Blossner and G. Clugston. "Worldwide timing of

- growth faltering: Implications for nutritional interventions". *Pediatrics*, vol. 107(5), May 2001.
- [10] Ernawati F, Rosmalina Y, Ridwan E, Permaesih D, Safitri A, Susilawati MD, Permanasari Y & Luciasari E. *Studi Longitudinal Faktor Risiko Terjadinya Stunting Pada Anak Bawah Dua Tahun [Laporan Penelitian]*. Bogor: Pusat Teknologi Terapan Kesehatan Dan Epidemiologi Klinik Balitbangkes RI. 2012.
- [11] Pusparini. F. Ernawati. Hardinsyah. D. Briawan. "IMT rendah pada awal kehamilan dan defisiensi vitamin A pada trimester kedua sebagai faktor risiko gangguan pertumbuhan linier pada bayi baru lahir". *Jurnal Gizi dan Pangan*, vol. 11(3), Nov. 2016
- [12] R.S. Gibson. *Principles of Nutritional Assessment*. Second Edition. New York: Oxford University Press, 2005.
- [13] A.J. Prendergast and J.H. Humphrey. "The stunting syndrome in developing countries". *Paediatrics and International Child Health*, vol. 34, pp. 250-265, Nov. 2014.
- [14] N.W. Solomons, M. Vassenaar, A.M. Chomat, C.M. Doak, K.G. Kaski and M.E. Scott. "Stunting at birth: recognition of early-life linear growth failure in the western highlands of Guatemala". *Public Health Nutrition*, vol. 18(10), pp: 1737-1745, Jul. 2015.
- [15] A.D. Stein, M. Wang, R. Martorell, S.A. Norris, L.S Adair, I. Bas, et al. "Growth patterns in early childhood and final attained stature: data from five birth cohorts from low- and middle-income countries". *American Journal of Human Biology*, vol. 22, pp: 353–359, 2010.
- [16] P. Svefors, A. Rahman, E.C. Ekström, A.I. Khan, E. Lindström, L.A. Persson LÅ, et al. "Stunted at 10 years. Linear growth trajectories and stunting from birth to pre-adolescence in a Rural Bangladeshi Cohort". *PLoS One*, vol. 11(3): e0149700, Mar. 2016.
- [17] C.G. Victora, L. Adair, C. Fall, P.C. Hallal, R. Martorell, L. Richter, et al. *Maternal and child undernutrition: consequences for adult health and human capital*. *Lancet*, vol. 371, pp. 340-357, Jan. 2008.
- [18] M.K. Schmidt, S. Muslimatun, C.E. West, W.Schultink and J.G.A.J. Hautvast. "Vitamin A and iron supplementation of Indonesian pregnant women benefits vitamin A status of their infants". *British Journal of Nutrition*, vol. 86, pp. 607–615, Nov. 2001.
- [19] W.Z.A. Mikhail, H.M. Sobhy, H.H. El-sayed, S.A. Khairy, H.Y.H. Abu Salem and M.A. Samy. "Effect of nutritional status on growth pattern of stunted preschool children in Egypt". *Academic Journal of Nutrition*, vol. 2(1), pp. 1-9, 2013.
- [20] C.T. Chasapis, A.C. Loutsidou, C.A. Spiliopoulou and M.E. Stefanidou. "Zinc and human health: an update". *Archives of Toxicology*, vol. 86(4), pp. 521-534, Apr. 2012.
- [21] M. Barbara. and A. Black. "Markers of Validity of Reported Energy Intake, The American Society for Nutritional Sciences". *J. Nutr* , vol. 133, pp. 895S-920S, 2003.