

# JOURNAL OF BIOMEDICINE AND TRANSLATIONAL RESEARCH

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Research Articles

## Association of Growth Velocity with Insulin-Like Growth Factor-1 and Insulin-Like Growth Factor Binding Protein-3 Levels in Children with a Vegan Diet

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### Article Info

History:

Received: 22 July 2019

Accepted: 06 Feb 2020

Available: 30 April 2020

### Abstract

**Background:** Vegan diet in children provides the benefit of reducing the risk of being overweight and improving the fat profile. However, the risk that may occur in the provision of a vegan diet in children is anthropometric size below normal range of reference and low caloric intake. Growth hormone (GH) and Insulin like Growth Factors (IGFs) are powerful stimulators for longitudinal growth of bone and require insulin-like growth factor binding protein (IGFBPs) which acts as a transport protein for IGF-1. Published research has shown that children who consume vegan diet has lower caloric intake and lower IGF-I levels than those on omnivorous diet.

**Objective:** To determine the effect of vegan diet on IGF-1 levels, IGFBP-3 levels, and growth velocity.

**Methods:** This was a prospective cohort study. The subjects were divided into two groups, namely the vegan group and the omnivorous group, then match based on age and sex. Anthropometric data collection, IGF-1 and IGFBP-3 levels measurements were done in both vegan and omnivorous children. Each subject was observed for 6 months starting in June 2018 and ending in February 2019.

**Results:** During 6 months of observation, 22 subjects were divided into two groups, a vegan diet group and an omnivorous diet group. The IGF-1 level in vegan children was  $105.5 \pm 47.3$  (ng/mL) compared to  $102.7 \pm 42.3$  (ng/mL) in omnivorous children with a p value of 0.89. IGFBP-3 in vegan children was  $2146.4 \pm 595.1$  (ng/mL) compared to  $2142 \pm 609.1$  (ng/mL) in omnivorous children with p value of 0.99 and growth velocity (cm/ 6 months) was 3.0 in vegan children (1.0-5.30), and 3.2 (2.6-6.5) in omnivorous children with a p value of 0.41.

**Conclusion:** Children with vegan diet had IGF-1 level, IGFBP-3 level, and growth velocity that were comparable to children with an omnivorous diet.

**Keywords:** IGF-1; IGFBP-3; Growth Velocity

**Permalink/DOI:** <https://doi.org/10.14710/jbtr.v6i1.5474>

### INTRODUCTION

Vegan diet in children and adolescents provides many benefits including reducing the risk of being overweight, reducing the risk of allergies, and improving fat profiles. However, according to Schurmann S. et al., in 2017, risks that may occur in children who consume vegan and vegetarian diet include anthropometry

measures below normal range of reference, low caloric intake, low vitamin D levels and low calcium levels.<sup>1</sup>

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In 1940, vegetarian population in England was 0.2%, which rose to 3 - 7% in the year 2000.<sup>2</sup> The vegetarian population in Shanghai in 2015 was around 0.77%, while in Germany, 2.1 - 6.1%, the United States 1.9 - 4% and in India, 36%.<sup>1,3,4,5</sup> The total population of vegetarians in Indonesia in 1998 was 5000 but in 2000 it increased to 60000.<sup>6</sup>

A recent study by Roman P et al. in 2017 showed that children with a vegetarian diet had lower mean height compared to non-vegetarian children. Causes of disturbances in growth velocity in vegan children were due to limited intake of essential proteins and amino acids, low insulin-like growth factor-I (IGF-1) and insulin-like growth factor binding protein (IGFBP-3) levels.<sup>10,11,12,13,14,15</sup>

Height growth occurs in the growth plate cartilage which is regulated by the work of an endocrine complex. Growth hormone (GH), IGF-1 and IGFBPs are the main endocrine complexes that play a role in growth. Growth hormone and IGFs are powerful stimulators for longitudinal growth of bone.<sup>16,17</sup> Insulin-like growth factors require transporters to the target tissue. Insulin-like growth factor binding protein works as a transport protein for IGF-1. Normal IGF-1 levels are needed for growth on the epiphyseal plate.<sup>18</sup> This comparative study aims to see the effect of vegan diets on IGF-1 levels, IGFBP-3 levels, and growth velocity of these children.

## MATERIAL AND METHODS

This study was a prospective cohort study conducted over six months. The study subjects were divided into two groups, namely those with a vegan diet and those with an omnivorous diet matched by age and sex. Anthropometric data collection, IGF-1 and IGFBP-3 levels measurements were done in both vegan and omnivorous children in selected communities upon recruitment. Subjects recruitment began in June 2018 and ended in February 2019. Subjects were observed starting from the first measurement and continued until six months.

The study population was children with a vegan diet or omnivorous diet aged 3 to 9 years who were in communities and schools in Denpasar, Surabaya and Balikpapan. Vegan children were selected from members of Supreme Master Ching Hai International Associations (SMCHIA) in Indonesia which required its members to be vegan. Omnivorous children were matched according to age and sex.

Universal sampling was done in this study. The inclusion criteria were vegan children aged 3 to 9 years old who had been consuming a vegan diet for at least 6 months. The exclusion criteria were children with growth disorders, children with malnutrition, children who consumed food supplementation, children with tall stature, children with short stature, children with bone deformities, children who were in the puberty phase (Tanner 2 or more) at the beginning of the study, children on growth hormone therapy, and children with syndromes that cause growth disorders.

The operational definition of vegan children was children with diet that excludes any animal products such as animal flesh (meat, poultry, fish and seafood) and animal products (eggs, dairy, honey) for 6 months or more.<sup>5,7,11,19,20</sup> Omnivorous or non-vegan children were

children who had consumed all types of foods and beverages made from animal and vegetable-based ingredients for more than once a week.<sup>21</sup> Height was the length of the body in a position of standing straight on the axis of the body from head to toe. Height was measured in cm. Height measurement was done barefoot. Heel, buttocks, shoulders, back and the back of the head must be in contact with the wall.<sup>22,23</sup> Height was measured once using OneMed brand stadiometer height gauge in all subjects with a level of accuracy to one decimal. IGF-1 levels were measured using the IMMULITE 2000 IGF-I machine. IGFBP-3 levels will vary according to age, sex and puberty status.<sup>24,25</sup> IGFBP-3 levels were measured using the Biorad ELISA Reader 680 machine.

The study was approved by the Ethics Committee of Faculty of Medicine, Universitas Airlangga-Dr. Soetomo Hospital number 29/EC/KEPK/FKUA/2018. Written informed consent was obtained from the parents. Interviews were then conducted to complete the study questionnaire and subsequently anthropometric measurements of height, IGF-1 and IGFBP-3 examinations were performed in the first month upon recruitment. After six months of observation repeated height measurements were done. Data were analyzed by SPSS for windows version 20.0.

## RESULTS

The sample of this study were 17 vegan children who met the study criteria; 6 children were excluded as there was no parental consent. Thus only 11 children were willing to participate in the study until completion.

The mean age of the study subjects in the vegan diet group was  $74.1 \pm 20.7$  months and in the omnivorous diet group,  $72.2 \pm 16.9$  months. The number and sex in both groups were similar.

During 6 months of observation, the 22 subjects were divided into two groups, a vegan diet group and an omnivorous diet group. There were no statistical differences between the age of the children (in months) and sex in the two study groups ( $p = 0.81$ ;  $p = 1,000$ ). IGF-1 values in children with a vegan diet and omnivorous diet were not statistically different. IGFBP-3 in children with a vegan diet and omnivorous diet were not statistically different (Table 1). Growth velocity in both groups was also not statistically significant ( $p > 0.05$ ) as listed in Table 1.

**Table 1.** Comparison of IGF-1 level, IGFBP-3 level and growth velocity

Variable	Vegan diet, n=11	Omnivorous diet, n=11	p
IGF-1 (ng/mL)	105.5 ± 47.3	102.7 ± 42.3	0.89
IGFBP-3 (ng/mL)	2146.4 ± 595.1	2142 ± 609.1	0.99
Growth Velocity (cm/6 months)	3.0 (1.0-5.30)	3.2 (2.6-6.5)	0.41

The value of IGF-1 and IGFBP-3 was in mean ± SD

Growth velocity was in median, min-max

Statistically significant if  $p < 0.05$

## DISCUSSION

The results of the study by Krupp D et al., in 2016, found that children aged 6 months to 19 years old with increased consumption of vegetables and fruits showed no difference in IGF-1 and IGFBP-3 levels.<sup>27</sup>

Randomized blinded clinical trial in vegan adults also gave similar results.<sup>28</sup> Vegan adults have the same calorie, total protein, zinc, selenium, magnesium, calcium, phosphate and potassium as non-vegetarians (omnivores).<sup>29,30,31,32</sup> Vegan children have consumption of protein, calcium, zinc which are according to the recommended daily requirements (RDA).<sup>34</sup>

Nutritional needs of children in Indonesia is based on the Indonesian Minister of Health Regulation No. 75 of 2013. Children's nutritional needs are adjusted for age and sex. Ernawati F et al. in 2016 showed that children aged 37 to 59 months consumed as much animal protein as 21.9 g / day and vegetable protein of 17.8 g / day or according to 139.8% from the mean adequacy ratio (MAR). The largest source of animal protein was from fish, milk (along with its processed products), eggs and meat or chicken. The most abundant source of vegetable protein comes from cereals, nuts and seeds.<sup>35</sup> Children aged 4 to 6 years in India has an average protein consumption of 47.3 g / day with a composition of 10 to 20% animal protein and 80 to 90% vegetable protein. The highest source of vegetable protein comes from cereals and grains while the largest source of animal protein comes from milk and its processed products.<sup>1,4,36</sup> Adequacy of nutrition for children with a vegan diet are similar to children with an omnivorous diet. Differences exist in fiber and protein intake which are slightly higher than the recommended dietary allowance (RDA) because of differences in protein absorption and amino acid composition.<sup>37,38,39</sup>

The number of calories and calcium consumed is related to the level of IGBBP-3.<sup>30,31</sup> In adults with a vegan diet, they have the same consumption of calories and calcium as in adults with omnivorous diet.<sup>12,31</sup> Vegetarian children have the same total calorie and calcium consumption as omnivorous children.<sup>11</sup> However, Hebbelink M et al., in 1999 showed contradictory results. Prepubertal vegetarian children in the Flemish group received lower caloric intake compared to the references. Male vegetarian children consumed  $6372 \pm 1297$  of calories (mean  $\pm$  SD), while the female children consumed  $5749 \pm 13393$  (mean  $\pm$  SD).<sup>40</sup>

A study by Haugen MA et al., in 1993 also showed that adults on a vegan diet for 3.5 months had reduced IGF-1 levels compared to adults on a normal (omnivorous) diet; this difference was however not statistically significant. On the other hand, Allen NE et al., in 2000, showed a significant reduction in IGF-1 level.<sup>41,42</sup>

In a study by O Connell JM et al., in 1988 in Tennessee, United States which included a group of vegetarian children aged 2 to 10 years, the growth rate of vegetarian and non-vegetarian children was similar according to the reference curve especially at the age of more than 5 years, while at the age of less than 5 years, the rate of height growth was lower in the vegetarian group and this was statistically significant.<sup>43</sup> Another study by Nathan I, in 1997 showed that growth velocity in vegetarian children aged 7 to 11 years ranged from 6.48 cm / year and 6.05 cm / year in omnivorous children but there was no statistical difference.<sup>22</sup> Our result showed that the vegan diet group has a lower growth velocity but was not statistically significant.

## CONCLUSION

Children with vegan diet had comparable though not similar IGF-1 and IGFBP-3 levels as children with omnivorous diet. Children with vegan diet had similar growth velocity as children with omnivorous diet. Further study is needed to determine the structure and mechanism of IGF-1 formed from amino acids from vegetable protein sources.

## ACKNOWLEDGMENTS

Our appreciation to Nur Rochmah from Department of Pediatrics, Division of Pediatric Endocrinology, Faculty of Medicine, Universitas Airlangga-Dr Soetomo Hospital, Indonesia who had given suggestions regarding the study.

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