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Deficiency of Serum Zinc in Children With Down Syndrome

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Abstract:

Down Syndrome (DS) is the most common chromosomal condition in Brazil, and represents the genetics anomaly with the highest prevalence in pediatrics. Higher incidence of several clinical complications and higher prevalence of mineral and vitamin deficiencies have been observed in children with DS. One of them, zinc is an essential micronutrient for human nutrition and health.However, little is known about the magnitude of this deficiency in children with DS in Brazil. The objective of this study was to evaluate nutritional level of zinc considering zinc serum levels and dietary intake of this micronutrient in children and adolescents with DS. Method: A cross-sectional clinical study was conducted, approved by the Research Ethics Committee. All children who underwent follow up at the Genetics Child Care outpatient ward of the University Hospital were eligible. Data were collected in 2017 and 2018. Dietary recall was taken and blood collection was performed for lab evaluation of serum zinc level of all participants. Values of serum zinc lower than 65 µg/dL were considered as deficiency. Results: A total of 37 children with DS were included. The analysis of serum zinc levels showed deficiency in 94.3% of the children, the mean zinc serum level was 50.40 µg/dL, median was 49.24 µg/dL (sd =10.1µg/dL). Only 5.4% of children presented deficiency in dietary intake of zinc. We concluded that incidence of inadequate zinc nutritional status in children with DS was high.

Keywords **—Children, Down Syndrome, Zinc.**

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I. INTRODUCTION

Down Syndrome (DS) is the most common chromosomal condition in Brazil, and represents the genetics anomaly with the highest prevalence in pediatrics [1].

Higher incidence of several clinical complications and higher prevalence of mineral and vitamin deficiencies have been observed in children with DS. One of them, zinc (Zn) is an essential micronutrient for human nutrition and health [2-4]. However, little is known about the magnitude of this deficiency in children with DS in Brazil, as the existing studies have been conducted with small and regionalized populations [5-7].

Zinc deficiency is related with increased morbidity and severity of infections, short stature, anorexia, dermatitis and jeopardized learning (as it acts in cognitive processes). It affects gustative perception and hormonal secretion related with the thyroid function, bone mineralization and reproduction. It has a crucial role in gene regulation, cell membrane stabilization and as an antioxidant[3,6,8,9].

Children with DS have higher prevalence of this deficiency, with losses and serious repercussions for their biochemical, immunological and clinical functions [3,5,7].

Therefore, the objective of this study was to evaluate nutritional level of zinc considering zinc serum levels and dietary intake of this micronutrient in children and adolescents with Down syndrome.

Method

A cross-sectional clinical study was conducted and approved by the Research Ethics Committee [name suppressed], Brazil (N°CAAE62014216.0.0000.5411).

All children who underwent follow up at the Genetics Child Care outpatient ward of the University Hospital [name suppressed] were eligible for the study. Data were collected in 2017 and 2018.

Children´s guardians were invited to participate and those who accepted the invitation signed the Informed Consent Form, and those who for any reason could not attend all the phases of the study were excluded. A total of 39 children were included, and as some of them did not agree to participate, the study was conducted with 37 children. In the results section, age groups were not differentiated in the analysis because of the "n" size. Only 2 of the total children included were adolescents, and for that reason, all included individuals considered throughout the text will be referred as children.

Dietary recall was taken and blood collection was performed for lab evaluation of serum zinc level of all participants.

Dietary recall was based on collection of 24-hour information from 3 consecutive days before doctor´s appointment, being at least one day of the weekend and one regular day. Evaluation of zinc dietary intake was performed using the Program of Nutrition Support - NutWin [software] [10]. Nutritional references, according to age group, to classify adequacy, deficiency or excess of dietary intake were based on Dietary Reference Intakes (DRIs) according to the National Research Council

(2000, 2002 e 2006) [11-13] as shown in Table 1. In the dietary recall, types of food consumed as zinc sources and foods which act as inhibitor of zinc absorption were identified.

Table 1. Dietary recommendation of zinc for children and adults according to the *Recommended Dietary Allowance* (RDA).

Age group	Zinc (mg/d)
0 – 5.9 months	2
6 – 11.9 months	3
1- 3.9 years	3
4 – 8.9 years	5
9 – 13.9 years (boys/girls)	8
14 -18 years (boys)	11
14 - 18 years (girls)	9

Source: *Recommended Dietary Allowances and Adequate Intakes (Food and Nutrition Board*, 2002) [12].

For analysis, zinc serum was obtained from plasma, and the collection was performed in the morning after a minimum 4-hour fast period. Whole blood was separated and centrifuged (4 ml collected). Sample preparation was performed using the mineralization methodology in microwave woven followed by analysis in an Atomic AbsorptionSpectrometer for qualiquantitative readings of Zn [14].

Values of serum zinc lower than 65 µg/dL were considered as deficiency for both sexes according to reference values established by the National Health and Nutrition Examination Survey [15].

Statistical Analysis

Chi-Square and Fisher's exact tests were used to study the association between variables.

Means were compared using the Student's T-test.

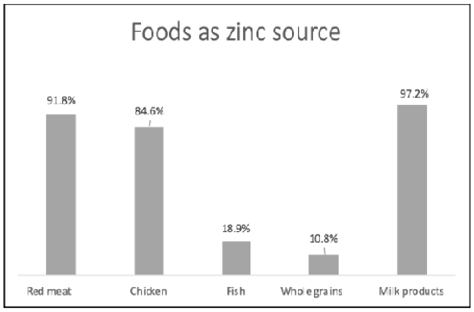
Differences and associations were considered significant for $p < 0.05$. SPSS (v10) statistical program was used in the study[16].

Results

Dietary recall was taken for 39 children followed by blood collection for serum zinc evaluation. In this step, 2 children were excluded because of an error in the outpatient care follow-up. Therefore, the final "n" was 37 participants. Because of a technical error during sample preparation, 2 samples were lost, and the study ended with serum analyses of 35 samples.

In relation to dietary intake of zinc, only two out of 37 participants (5.4%) had deficiency in the dietary intake of this micronutrient.

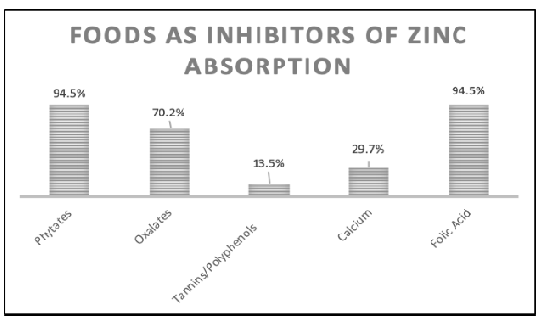
Graphic 1 shows main types of foods consumed as source of dietary zinc. Milk products were the main consumption, 97.2% (n=36), followed by red meat, 91.8% (n=34) and chicken, 86.4% (n=32). Other sources of less consumption were as follows: fish 18.9% (n=7), whole grains 10.8% (n=4) and liver 5.4% (n=2).



Graphic 1. Groups of foods consumed as zinc source.

Groups of foods consumed as zinc source.

The main consumed foods which act as inhibitors of zinc absorption were phytates and folic acid. They were consumed by 94.5% (n=35) of the participants. The foods as oxalate source were consumed by 70.2% (n=26). The least consumed foods were those as source of calcium 29.7% (n=11), tannin and polyphenol 13.5% (n=5).



Graphic 2 . Groups of consumed foods as potential inhibitors of zinc absorption.

Group of consumed foods as potential inhibitors of zinc absorption.

Children with insufficient dietary intake of zinc also consumed inhibitor foods of zinc absorption (table 2).

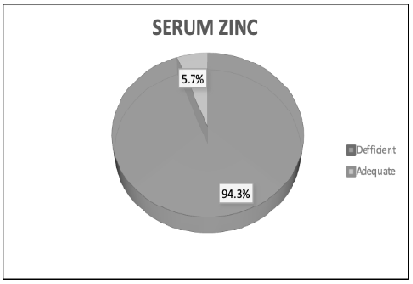
Table 2.Dietary intake of zinc absorption inhibitors in children and adolescents with Down syndrome.

Dietary Zinc	Food inhibitors of zinc absorption: No	Yes	Total	p-value
	N (%)	N (%)	N (%)	
Adequate	16 (47.0)	18 (53.0)	34 (100.0)	0.19
Insufficient	0 (0.0)	2 (100.0)	2 (100.0)	
Total	16 (44.4)	20 (55.6)	36 (100.0)	

A total of 35 children (one adolescent) presented deficiency 94.3%, in the analysis of serum zinc levels. Mean zinc serum level was 50.40 µg/dL, median was 49.24 µg/dL (SD =10.1µg/dL). Only 5.7% of participants presented normal values of serum zinc (graphic 3).

Classification of serum zinc levels in children with Down syndrome.

The joint analysis of zinc serum level and dietary intake showed that children with deficient zinc serum level had adequate dietary intake of Zinc in its entirety ($p < 0.001$), as shown in Table 3.



Graphic 3. Serum zinc in children with Down syndrome.

Table 3. Adequacy of zinc serum level and intake of zinc source foods in children and adolescents with Down syndrome.

Serum zinc	Intake of zinc source food			p-value
	Adequate	Insufficient	Total	
	N(%)	N(%)	N(%)	
Adequate	1(50.0)	1 (50.0)	2 (100.0)	< 0.0001
Insufficient	33(100.0)	0 (0.0)	33 (100.0)	
Total	34(97.1)	1 (2.9)	35 (100.0)	

Table 4 shows that the relationship between dietary intake of zinc absorption inhibitors and adequacy of zinc serum levels was not statistically significant (p = 0.17).

Table 4.Adequacy of zinc serum level and intake of potentially inhibitor foods of zinc absorption.

Serum zinc	Inhibitor foods			p-value
	No	Yes	Total	
	N(%)	N(%)	N(%)	
Adequate	0(0.0)	2(100.0)	2(100.0)	
Insufficient	16(50.0)	16(50.0)	32(100.0)	0.17
Total	16(47.0)	18(53.0)	34(100.0)	

Discussion

The main result obtained in this study was the deficiency of serum zinc level even with dietary intake of Zinc by the children not being insufficient. However, dietary intake of zinc does not guarantee cell utilization of this micronutrient, as there may be chemical interactions with other substances, such as oxalates, phytates, fibers and some minerals which affect absorption [5,6,17,18], including the high intake of milk and dairy products found in another study in Brazil [20].

Other factors besides diet may also affect absorption, capturing and cellular transport of zinc, such as genetic and systemic factors, state of anabolism and catabolism, endocrine changes, liver function, renal function, stress and infections [7,17].

In view of the high prevalence of zinc serum deficiency, concerns exist about its repercussions, as zinc acts in cell metabolism, with consequences for almost all organs and systems of the human body, improving mental and psychomotor development, reducing morbimortality and extenuating negative repercussions in biochemical , immunological and clinical functions, in case of its deficiency not being treated [2,3,5,6].

Many studies in the literature report that the nutritional status related with zinc in children with DS has different characteristics in comparison with that in children with no DS. Changes in the antioxidant, immunological systems and hormonal metabolism as a result of changes in the nutritional status of zinc have not reached a consensus yet [2,3,5]This fact may explain the zinc deficiency in the dietary intake observed in our study with normal values of zinc serum levels.

Some studies have already reported metabolic and biochemical changes which predispose those with DS to zinc deficiency. Because of trisomy 21, changes occur in the tissue diffusion of zinc and an increase of 50% is observed in the expression of genes which transcribe the copper, zinc superoxide dismutase (or Cu, Zn SOD) enzyme, increasing its intracellular activity [2,3,5,7,17] These findings corroborate our results, in which, even children and adolescents, who had diet with adequate level of zinc, showed serum deficiency of this micronutrient.

Clinical manifestations of zinc deficiency may vary within a wide range from minor to more serious manifestations. They could be attributed to the genetic condition itself [2,6]. Therefore, further studies should be conducted for better understanding of the clinic-laboratorial zinc correlation, as this micronutrient is of crucial importance in some clinical manifestations in people with DS.

Based on the importance of this micronutrient for adequate growth and development, these children should have careful and comprehensive follow-up in their routine appointments with special attention to that condition.

Healthy feeding enables adequate growth and development, optimizing the function of organs and systems and preventing diseases in the short and long term. On the other hand, inadequate feeding is one of the most important factors which contribute towards the onset of chronic-degenerative diseases, which are nowadays the major cause of morbimortality in adults. The increased number of these diseases is related with the life style adopted since childhood, including inadequate feeding habits with high intake of carbohydrates, industrialized foods, sugar, fat, and low intake of micronutrients, mainly zinc [17,19,20].

Increased survival rate was observed in people with trisomy, so that further studies using new therapeutic procedures are needed for comorbidity prevention and health promotion. This differentiated outlook will bring a holistic vision with improvement in life quality and promotion of functional gains and positive changes throughout the years. Moreover, it will provide integral health care to people with DS, so that individual development will reach its full potential with benefits to society and health services.

As the study limitations, we point out the number of included individuals. However, because of being a specific population, we must consider that only wider and multicenter studies would enable a larger number of included individuals. Other study limitation was the analysis of only serum level of zinc although, it is nowadays, the most used index to evaluate nutritional status of this mineral. Also, it presents a fast response to any variation of this mineral. Many authors do not consider serum level of zinc as a reliable parameter when used alone, and they suggest using it in combination with other indicators, like erythrocyte zinc, among others [2,7,17].

More advanced clinical studies, including erythrocyte zinc level and comparison with a non-DS control group, should help understanding zinc levels in these children population. We also observed the need for further studies to shed light on the metabolism changes of the micronutrient and specific needs of dietary intake from those with DS. These studies will advance nutritional and supplementation interventions for these children, as current studies on these issues in Brazil are rare [5,6].

We concluded that deficiency of serum zinc in children with DS had high incidence, however with no relationship with dietary intake of this micronutrient, thus indicating that there is an inadequate zinc nutritional status in children with DS. Therefore, we considered the biochemical and metabolic changes reported in children with DS as a possibility to explain serum insufficiency of Zinc. Supplementation of this micronutrient could be suggested to prevent deficits and their consequences to the body, and promote adequate growth and development of those with DS.

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Conflict of interests

The authors certify that there is no conflict of interest.

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