

# Biochemical and hematological evaluation in subjects with intellectual disability associated or not to Down syndrome

## *Avaliação bioquímica e hematológica em indivíduos com deficiência intelectual associada ou não à síndrome de Down*

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### ABSTRACT

Down syndrome (DS) is one of the most leading causes of intellectual disability. The aim of this study was to compare biochemical and hematological parameters, triglyceride/high-density lipoprotein cholesterol (HDL-C) and neutrophil/lymphocyte ratios in individuals with intellectual disabilities (ID) associated or not with DS. The main result is the lower HDL-C level in individuals with DS than in the ID group, suggesting a modification in the lipid profile whose origin would lie in genetic alterations. However, further researches are important to analyze if there is any link between trisomy 21 and the reduction of plasma HDL-C levels in individuals with DS.

**Key words:** Down syndrome; trisomy; intellectual disability; mentally disabled persons.

### INTRODUCTION

The main cause of intellectual disability (ID) are chromosomal alterations, with Down syndrome (DS) being the most frequent one<sup>(1)</sup>. DS is a genetic change resulting from an extra copy of chromosome 21, characterized by delayed psychomotor development<sup>(2)</sup>.

In addition, individuals with DS may present with specific health problems such as congenital heart diseases, diabetes, renal disease, hematological abnormalities, obesity and premature aging<sup>(3-6)</sup>. This population shows a disadvantage compared to individuals with ID without DS, which have a longer life expectancy<sup>(7)</sup>.

Thus, it becomes interesting to compare laboratory tests among individuals with IDs associated or not with DS. The aim of this study was to compare biochemical and hematological parameters, triglyceride/high-density lipoprotein cholesterol (HDL-C) and neutrophil/lymphocyte ratios in individuals with IDs associated or not with DS.

### MATERIAL AND METHODS

The subjects were selected from a service for individuals with special needs, in Ponta Grossa (PR). A case-control study was carried out with two groups: group I (DS) – volunteers with DS; and group II (ID) – volunteers with other IDs.

The legal guardians of the participants were informed about the survey and freely signed and dated the consent form. The protocol was approved by the Ethics in Research Committee of Universidade Estadual de Ponta Grossa (UEPG) (75/2009) and was conducted in accordance with the Helsinki Declaration.

#### **Hematologic and biochemical parameters**

Complete blood count (CBC) was performed by Hemacounter 60-RT 7600<sup>®</sup> hematological counter (Hemogram, Brazil).

The levels of glucose, total cholesterol and triglycerides (enzyme-Trinder method), HDL-C (colorimetric method without

precipitate), creatinine (Jaffe reaction) and urea (colorimetric method) were obtained by using the automated analyzer respos<sup>®</sup> 920 and standardized kits (DiaSys Diagnostic Systems<sup>®</sup>). Low-density lipoprotein cholesterol (LDL-C) levels were calculated using the Friedewald equation: LDL-C = total cholesterol - HDL-C - (triglycerides/5)<sup>(8)</sup>, when triglyceride levels were below 400 mg/dl; and non-HDL-C, calculated by the formula: total cholesterol - HDL-C<sup>(8)</sup>. Glycated hemoglobin (HbA1c) was measured by high-performance liquid chromatography (HPLC) in a Diafast<sup>®</sup> analyzer (Prime Diagnostics, USA).

### Triglyceride/HDL-C and neutrophil/lymphocyte ratios

Triglyceride/HDL-C ratio was calculated by dividing plasma concentrations of triglycerides by HDL-C values. Neutrophil/lymphocyte ratio was obtained by dividing neutrophil absolute count by lymphocyte absolute count in the peripheral blood.

### Statistical analysis

Normality of data was assessed by the Shapiro-Wilk test. For the variables that did not present normal distribution, the logarithmic transformation was applied before the parametric analysis. Possible differences between the groups were evidenced by Fisher's exact test for the categorical variables and by *t*-Student test for the continuous variables. In all tests, the level of significance was pre-set at < 0.05. Data were analyzed by statistical software SPSS 17.0<sup>®</sup> (Chicago, USA).

## RESULTS

The study population consisted of 37 children and adolescents. The group with ID presented individuals with a median age of 15 (14-17) years, 17 (63%) males and 10 (37%) females; whereas the group with DS presented individuals with a median age of 14 (13-18) years, six (60%) males and four (40%) females. There was no statistically significant difference for variables age ( $p = 0.641$ ) and sex ( $p = 0.579$ ) between the groups, demonstrating the homogeneity of the studied population.

The **Table** shows the results of the biochemical analysis and triglyceride/HDL-C and neutrophil/lymphocyte ratios. The group with DS presented significant decrease only in HDL-C levels ( $p = 0.034$ ) compared to the ID group.

**TABLE – Biochemical parameters, triglyceride/HDL-C and neutrophil/lymphocyte ratios in the groups ID and DS**

Parameters	ID (n = 27)	DS (n = 10)	p-value
Glucose (mg/dl)	87 (84-92)	89 (83-106)	0.576
Glycated hemoglobin (%)	5 (4.7-5.3)	5.6 (4.8-5.8)	0.056
Cholesterol (mg/dl)	145 (133-183)	143 (123-165)	0.295
Triglycerides (mg/dl)	75 (59-101)	87 (55-101)	0.387
HDL-C (mg/dl)	46 (38-54)	40 (33-42)	0.034*
LDL-C (mg/dl)	87 (66-113)	86 (73-113)	0.821
Non-HDL-C (mg/dl)	100 (82-133)	97 (81-125)	0.684
Creatinine (mg/dl)	0.82 (0.71-0.9)	0.83 (0.77-0.98)	0.181
Urea (mg/dl)	27 (21-32)	29 (27-37)	0.255
Triglycerides/HDL-C	1.67 (1.26-2.31)	1.87 (1.27-2.81)	0.242
Neutrophil/lymphocyte	1.51 (1.03-1.93)	1.86 (1.05-2.62)	0.301

Values are medians and interquartile ranges, *t*-Student test; \*significant difference from the control group ( $p < 0.05$ ).

HDL-C: high-density lipoprotein cholesterol; ID: intellectual disability; DS: Down syndrome; LDL-C: low-density lipoprotein cholesterol.

Hematologic parameters were also compared between the groups. The results were significantly different ( $p = 0.019$ ) for mean corpuscular volume (MCV) with 87 fl (86-88 fl) for the ID group, and 91 fl (87-92 fl) for the DS group. Absolute eosinophil counts and absolute band counts also were significantly different ( $p = 0.042$ ,  $p = 0.036$ , respectively). The red blood cell counts, hemoglobin, hematocrit, mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), total leukocytes, monocytes, lymphocyte, segmented, neutrophil, and platelet absolute counts were not statistically different between the analyzed groups.

## DISCUSSION

The presented results agree with a previous study comparing DS children with their siblings, between 4 and 10 years of age, demonstrating decreased HDL-C levels in DS individuals<sup>(9)</sup>. In addition, this study also reported increased values for triglycerides, total cholesterol and LDL-C, demonstrating an unfavorable lipid profile in individuals with the syndrome, regardless of weight conditions<sup>(9)</sup>.

Moreover, a study involving 138 children, including 72 children with DS, also presented similar results with reduced HDL-C levels, as well as elevated concentrations of total cholesterol, triglycerides and LDL-C in children with DS<sup>(10)</sup>. This study suggests that changes in lipid metabolism found in children with DS may be determined by unknown genetic alterations<sup>(10)</sup>.

However, recent studies reported no differences in lipid profile between subjects with DS and healthy controls. Tansley *et al.* (2012)<sup>(11)</sup>

studied 20 adults with DS. They were compared to healthy controls and their lipid profiles were similar, suggesting that trisomy 21 does not alter significantly the lipid metabolism. Another study, developed by Real de Asua *et al.* (2014)<sup>(12)</sup>, compared 49 adult subjects presenting DS to 49 healthy controls, and showed no difference between the groups for cholesterol, triglycerides, HDL-C and LDL-C.

In the present study, no differences were observed as to glucose and HbA1c between individuals with DS and DI (Table). Some studies have shown that individuals with DS are more likely to present diabetes *mellitus*, either by an autoimmune disorder (mostly type 1 diabetes *mellitus*) or by insulin resistance (mostly type 2 diabetes *mellitus*)<sup>(13)</sup>. It must be noted that the present study showed HbA1c results for individuals with DS indicative of high risk for developing diabetes (HbA1c between 5.7% and 6.4%)<sup>(14)</sup>, what could suggest a tendency to develop diabetes in the future.

Regarding the analysis of renal function, the current study does not present results outside the reference ranges for creatinine and urea; likewise, there was no difference between individuals with DS or ID. However, a similar study found that individuals with DS had higher creatinine levels compared to individuals with ID<sup>(15)</sup>. Another study in adults with DS compared with healthy controls demonstrated increased levels of creatinine in individuals with DS<sup>(16)</sup>.

The present study also demonstrated an increase in MCV values in the DS population, suggesting a tendency for macrocytosis. Several studies have demonstrated the increase in MCV in individuals with DS<sup>(17,18)</sup> and remaining elevated values throughout life for two-thirds of this population, what may hinder the interpretation of red blood cell (RBC) indices for the diagnosis of anemia<sup>(19)</sup>.

In addition to the highest tendency towards macrocytosis, several studies have evaluated the hematological profile in individuals with DS. Tenenbaum *et al.* (2011)<sup>(20)</sup> demonstrated that children with DS (aged 0-20 years) are at high risk for the development of iron deficiency anemia, as is the case with children in the general population. Awasthi *et al.* (2005)<sup>(21)</sup> evaluated 239 children with DS during a period of 10 years, and 6.2% of them presented some type of hematological disease, such as acute leukemia, transient myeloproliferative disease (73.3%), or anemia (1.7%). Taub (2001)<sup>(22)</sup> reported the highest risk of developing acute lymphoblastic leukemia (ALL) or acute myelogenous leukemia (AML) faced by children with DS, compared to children without the syndrome.

Regarding the hematological parameters in DS, the reference values for hematological indices of children with DS are within the range established for children without the syndrome, what is supported by a study developed in Brazil, with children aged 2 to 10 years who did not present clinical signs and/or symptoms of infectious diseases<sup>(23)</sup>.

The triglyceride/HDL-C ratio is a suitable marker for the identification of children with cardiovascular risk<sup>(24)</sup>. The present study results are in agreement with a previous study in the general population evaluating the triglyceride/HDL-C ratio for 6.197 children aged 10 to 19 years, in which the mean overall rate ratio was  $1.74 \pm 1.22$ <sup>(25)</sup>. The values obtained for individuals with ID associated or not with DS, evaluated in the present study, were similar to those found in children in the general population.

Another relationship that is currently associated with an unfavorable cardiovascular profile in children is the neutrophil/lymphocyte ratio<sup>(26)</sup> but we found no difference between individuals with ID and DS.

The main result is the decreased HDL-C level in individuals with DS when compared to the ID group, suggesting a modification in the lipid profile whose origin would lie in genetic alterations. However, the study presents important limitations regarding the sample size of the groups and confounding variables for a case-control study such as age and gender that were not paired, although the homogeneity of the population was statistically proved.

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## CONCLUSION

Comparing the laboratory tests of individuals with ID and DS, the present study showed that there are no major differences between the two populations, except regarding the plasma levels of HDL-C. In this study, decreased levels of HDL-C were observed only in individuals with DS. The present study revealed possible higher risk for DS subjects to develop diabetes in the future through the HbA1c values observed. However, due to the limitations of the study, such as the small sample size, further researches are important to analyze if there is any link between trisomy 21 and the decreasing plasma HDL-C levels in individuals with DS.

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## CONFLICTS OF INTEREST

The authors declare no conflict of interest in any aspect of this report.

## RESUMO

*A síndrome de Down (SD) é uma das principais causas de deficiência intelectual. Os objetivos deste estudo foram comparar parâmetros bioquímicos e hematológicos, bem como encontrar a relação triglicérido/colesterol da lipoproteína de alta densidade (HDL-C) e a razão neutrófilo/linfócito em indivíduos com deficiência intelectual (DI) associada ou não à SD. O principal resultado foi a diminuição do HDL-C em indivíduos com SD quando comparados àqueles com DI, sugerindo que essa modificação no perfil lipídico pode se relacionar com alterações genéticas. Portanto, pesquisas adicionais são importantes para analisar se existe ligação entre a trissomia 21 e a redução dos níveis de HDL-C em indivíduos com SD.*

*Unitermos: síndrome de Down; trissomia; deficiência intelectual; indivíduos com deficiência mental.*

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