A STUDY OF BLOOD LIPID PROFILE IN CHILDREN WITH DOWN SYNDROME COMPARED TO OTHER CHILDREN

By

Ali Mohammed Abd El-Rahman Abdou*, El-Sayed Mohammed El-Nagar*, Ibrahim Mohammed Abou-Farag* and Eman Tayee El-Sayed**

Pediatrics* and Clinical Pathology** Departments, Faculty of Medicine, Al Azhar University, Cairo, Egypt

Composed author: Ali Mohammed Abd El Rahman Abdou

Mobile: 01202223105, **E-mail:** doctoralisu@gmail.com

ABSTRACT

Background: *Down syndrome (DS) is one of the most common causes of developmental disability in the world with a prevalence of 1:800 live births. Persons born with DS are at increased risk for various health conditions, including thyroid disease, leukemia, congenital heart defects, gastrointestinal tract abnormalities, obesity, and diabetes mellitus. Despite this increased risk of chronic disease, life expectancy for individuals with DS has continued to improve with an estimated mean survival approaching 60 years of age.*

Aim and objectives: *To study lipid profile in patients with Down syndrome compared to normal children.*

Subjects and methods: *This is a cross sectional analytic study that was carried out on a total of 100 children; 50 children previously diagnosed as Down syndrome by karyotyping and attending Bab Al sharia University Hospital and Alexandria University Hospital, and 50 healthy children as a control group during the period from February 2021 to January 2022, they were selected by simple random method. All studied children were subjected medical history (with special emphasis on age, sex and family history of ischemic heart disease or cerebrovascular accidents), clinical examination (with special emphasis on weight, height, body mass index and blood pressure) and laboratory investigations (TC, HDL, TG and LDL).*

Results: *Down syndrome cases had values of triglyceride statistically higher than healthy children. DS had values of cholesterol and low-density lipoprotein statistically higher than healthy children. Healthy children had values of high-density lipoprotein statistically higher than DS. We found no correlation between sex and different elements of lipid profile within Down syndrome group and no correlation between age and different elements of lipid profile within the two groups.*

Conclusion: *Down syndrome cases had values of triglyceride, cholesterol, and low density lipoprotein statistically higher than healthy children. Healthy children had values of high density lipoprotein statistically higher than DS.*

Keywords: Down syndrome, lipid profile.

INTRODUCTION

Down syndrome (DS) is one of the most common causes of developmental disability in the world with a prevalence of 1:800 live births. It is named after John Langdon Down, the British physician who described the syndrome in 1866. DS was identified as a chromosome 21 trisomy by Dr. Jérôme Lejeune in 1959; it can be identified in a baby at birth, or even before birth by prenatal screening **(Roizen and Patterson, 2013)**.

The average full-scale intelligence quotient (IQ) of young adults with Down syndrome is around 50 (70 and below is defined as the cut-off for intellectual disability), whereas healthy young adult controls have an average IQ of 100. It is typically associated with physical growth delay, a particular set of facial characteristics and a severe degree of intellectual disability **(Grant et al., 2010)**.

Persons born with DS are at increased risk for various health conditions, including thyroid disease, leukemia, congenital heart defects, gastrointestinal tract abnormalities, obesity, and diabetes mellitus. Despite this increased risk of chronic disease, life expectancy for individuals with DS has continued to improve with an estimated mean survival approaching 60 years of age **(Glasson et al., 2012)**.

Many children with Down syndrome are educated in regular school classes while others require specialized educational facilities. Some children graduate from high school, and, in the US, there are increasing opportunities for participating in post-secondary education. Education and proper care has been shown to improve quality of life significantly. Many adults with Down syndrome are able to work at paid employment in the community, while others require a more sheltered work environment **(Calefati, 2013)**.

Increasing life expectancy along with an elevated risk of obesity and diabetes mellitus in individuals with DS, raise concerns about long-term health, in particular, atherosclerotic cardiovascular disease. Obesity and insulin resistance, which are common among individuals with DS, are associated with unfavorable (more atherogenic) lipid profiles, characterized by high triglycerides (TGs) and low high-density lipoprotein (HDL)

cholesterol **(Pueschel et al., 2005)**.

With regard to the lipid metabolism of people with DS, **Adelekan et al. (2012)** compared serum lipid profiles, total cholesterol (TC), low-density lipoprotein (LDL), triglycerides (TG), and high-density lipoprotein (HDL) between children with Down syndrome (DS) and their non-DS siblings. They found that children with DS have less favorable lipid profiles than their siblings independent of weight status.

AIM OF THE WORK

The aim of this work is to study the lipid profile in patients with Down syndrome compared to normal children.

Sample size:

The study was conducted on a total of 100 children; these comprised 50 children previously diagnosed as Down syndrome by karyotyping and attending Bab Al Sharia University Hospital and Alexandria University Hospital, and 50 healthy children as a control group.

This study is based on a study carried out by **MujganSonmez et al., 2006**. Epi Info STATCALC was used to calculate the sample size by considering the following assumptions: - 95% two-sided confidence level, with a power of 80%. & an error of 5%. The final maximum sample size taken from the Epi- Info output was 94. Thus, the sample size was increased to 100 children to assume any drop out cases during follow up:

$$x = Z(c/100)\ ^2\ r\ (100-r)$$

$$n = N\ x/\ ((N-1)\ E2 + x)$$

$$E = Sqrt\ [(N - n)\ x/n\ (N-1)]$$

Where N is the population size, r is the fraction of responses that you are interested in, and Z(c/100) is the critical value for the confidence level c.

Ethical Considerations:

1. The study was done after being approved by the Institutional Ethical Committee, Al-Azhar University.
2. Informed consent was obtained from the parents before enrollment of the study.
3. All data was kept confidential.
4. All participants have the right to withdraw from the study without affecting their management.
5. No conflict of interest regarding the study publication.
6. Financial disclosure, the researcher declared that there is no fund regarding the study publication.

PATIENTS AND METHODS

This is a cross sectional analytic study that was carried out on a total of 100 children; 50 children previously diagnosed as Down syndrome by karyotyping and attending Bab Al sharia University Hospital and Alexandria University Hospital, and 50 healthy children as a control group during the period from February 2021 to January 2022, they were selected by simple random method.

Inclusion criteria:

1. Age between 4 and 10 years for all children.
2. Body mass index below the 85th percentile for age and sex.

Exclusion criteria:

1. Congenital cardiac defect requiring open heart surgery.
2. History of intestinal anomalies requiring bowel resection and/or ongoing medical intervention.
3. History of hypothyroidism.
4. History of malignancy.
5. Chronic conditions known to affect energy balance or growth, including diabetes mellitus.

Methods:

All patients were subjected to:

1. Complete history taking:

With stress on age, sex and family history of ischemic heart disease or cerebrovascular accidents.

2. Clinical examination:

With special emphasis on weight, height, body mass index and blood pressure and manifestations of down syndrome

3. Laboratory studies:

Blood samples were drawn from each child after fasting for 9-12 hours for total cholesterol (TC), high density lipoprotein (HDL), triglycerides (TG), and low density lipoprotein (LDL) by micro lab 300 2021 (Netherland), Human kits (Germany).

Serum samples were stored at –70°C until the time of analyses. Serum cholesterol levels were measured by a cholesterol oxidase enzymatic method, triglycerides by a glycerol oxidase enzymatic method, high-density lipoprotein cholesterol by a cholesterol oxidase enzymatic method in the supernatant after precipitation with phosphor-tungstic acid–$MgCl_2$, low-density lipoprotein cholesterol by the Fried Ewald formula (total cholesterol –

triglycerides/5+ high-density lipoprotein cholesterol).

Statistical analysis:

Statistical analysis was done using the SPSS software package version 23. Statistical analysis was done to obtain the mean, the standard deviation; the standard error of each mean and for comparison between the different groups involved in this study ONE WAY test was used for comparison between independent samples.

RESULTS

Our results were demonstrated in the following tables:

Table (1): Demographic and clinical finding on studied groups

	Group I Down syndrome		**Group II Normal children**		**Test of sig.**
	No	**%**	**No**	**%**	
Sex					
Female	20	40.0%	30	60.0%	X^2=2.68
Male	30	60.0%	20	40.0%	P=0.110
	(n=50)		(n=50)		
AGE					
Range	4.00-10.00		5.00-10.00		t=0.006
Mean±SD	8.2800 ±1.88237		8.2400 ±1.66533		P=0.937
BMI					
Range	15.00-20.00		14.50-19.00		t=2.054
Mean±SD	7.3160±1.30310		16.3520±1.12254		P=0. 087
SBP					
Range	80.00-90.00		80.00- 95.00		t=.096
Mean±SD	86.2000±3.89444		86.6000±5.14782		P=0.758
DBP					
Range	50.00- 70.00		50.00- 75.00		t=0.480
Mean±SD	61.0000±3.81881		62.0000±6.12372		P=0.492

There were no statistical significant differences between the two studied groups regarding sex, age, BMI, SBP and DBP.

Table (2): Lipid profile in both groups

		N	Min. in mg/dl	Max. in mg/dl	Mean	Std. Deviation	T	P
TGS	**Group I DS**	50	51.00	223.00	117.3200	43.93529	29.369	.0001*
	Group II Normal children	50	52.00	90.00	68.2000	11.11306		
TC	**Group I DS**	50	149.00	196.00	168.3200	13.02472	5.265	.009*
	Group II Normal children	50	133.00	180.00	151.2800	10.90950		
LDL	**Group I DS**	50	84.00	141.00	101.9600	12.48159	4.89	0.009*
	Group II Normal children	50	29.00	123.00	81.9600	15.39137		
HDL	**Group I DS**	50	21.00	62.00	41.0000	16.69581	5.055	.011*
	Group II Normal children	50	35.00	112.00	52.8800	8.82855		

Our study found that down syndrome cases had values of triglyceride, cholesterol and low-density lipoprotein statistically higher than healthy children. Healthy children had values of high-density lipoprotein statistically higher than down syndrome.

Table (3): Relation between sex of the patients and the lipid profile in group I

		Mean	S.D.	Min.	Max.	t-test	P
TRIG	Male	124.1053	47.43170	51.00	223.00	1.964	.174
	Female	95.8333	20.91331	65.00	120.00		
CHOL	Male	167.0000	12.92285	149.00	196.00	.807	.378
	Female	172.5000	13.61984	150.00	190.00		
LDL	Male	100.1053	10.40777	84.00	115.00	1.807	.192
	Female	107.8333	17.41742	85.00	123.00		
HDL	Male	44.6842	18.77070	21.00	112.00	.128	.724
	Female	41.8333	7.88458	34.00	53.00		

Table (3) shows that there was no correlation between sex and different elements of lipid profile within Down syndrome group.

Table (4): Correlations between age and lipid profile in the two studied groups

Age #		Group I Down syndrome	Group II Normal children
TRIG	Pearson Correlation	.002	.139
	Sig (2-tailed)	.993	.507
CHOL	Pearson Correlation	.045	.356
	Sig (2-tailed)	.832	.081
LDL	Pearson Correlation	.049	.046
	Sig (2-tailed)	.816	.829
HDL	Pearson Correlation	.083	.060
	Sig (2-tailed)	.693	.777

Table (4) shows that there was no correlation between age and different elements of lipid profile within the two groups.

DISCUSSION

Down syndrome (DS) is one of the most common causes of developmental disability in the world with a prevalence of 1 in every 800 live births **(Roizen and Patterson, 2013)**. who did not support describing DS as an atheroma-free model of disease found in the autopsy material of institutionalized children <21 years of age, slightly more atherosclerosis in the coronary arteries and aortas of persons with DS in comparison with other residents with intellectual disability(ID). They suggested that individuals with DS may actually have an increased risk of mortality from ischemic heart disease and cerebrovascular disease compared with the general population.

Our study was conducted on a total of 100 subjects aged from 4-10 years, these comprised 50 children previously diagnosed as Down syndrome by karyotyping and attending Bab Al Sharia University Hospital and Alexandria University Hospital for follow up, and 50 healthy children as a control group. Blood samples were drawn from all children after fasting for 9-12 hours and tested for total serum cholesterol (TC), high density lipoprotein (HDL), triglycerides (TG), and low density lipoprotein (LDL).

Results of our study suggested that the lipid profile of non-obese prepubertal children with DS is less favorable than that of normal children, with higher concentrations of total cholesterol (TC), low density lipoprotein

(LDL), and triglyceride (TG) and lower concentrations of high density lipoprotein (HDL).This unfavorable lipid profile may make these population at increased risk for ischemic heart disease and cerebrovascular accidents. Our findings of increased TC, LDL, TG, and decreased HDL in individuals with DS are similar to two previous reports. **Tahira et al. (2014)** studied lipid profile of 27 children with DS and 31 children of their normal siblings. Children with DS were found to have higher TG, TC, LDL, and lower HDL compared with normal siblings. They concluded that Children with DS have less favorable lipid profiles than their siblings independent of weight status. These findings may have important implications for the screening and treatment of this large population at increased risk for ischemic heart disease.

In a study done on 4800 individuals from Sweden and Denmark, individuals with DS were found to have a 3.9-fold increased incidence of mortality due to ischemic heart disease, the participants were selected through a hospital-based registry **(Hill et al., 2013)**. Also, another epidemiological study of 14,000 individuals in California found a similar 4.3-fold increased incidence of mortality due to ischemic heart disease. In this study, participants were selected from a state department of developmental services registry **(Day et al., 2015)**.

Other studies of lipid and lipoprotein concentrations in individuals with DS have produced varying results. A study performed by **Pueschel et al. (2005)** revealed no significant differences between the study and control groups as regard to total cholesterol, LDL cholesterol, apo B and the apo B: apo AI ratio. However, triglyceride levels were significantly increased, and serum HDL cholesterol, apo AI and HDL cholesterol: total cholesterol ratio was significantly decreased in patients with Down's syndrome when compared to the control group. The latter observations were all associated with an increased risk for coronary artery disease.

Dörner et al. (2010) have performed a study on 186 patients with Down's syndrome (age 1-68 yr) compared to 51 non-DS mentally handicapped adults living in the same institution as a control group. In this study it was found that patients' total cholesterol, beta-cholesterol and triglycerides did not differ from the controls. However, alpha-cholesterol was significantly lower

and the beta/alpha-lipoprotein ratio significantly higher in patients with Down syndrome, findings which are associated in the general population with a high risk for premature atherosclerosis.

The mechanism by which individuals with DS develop a less favorable lipid profile than normal children seems to be unclear, but based on our results, this mechanism does not appear to be explained by overall adiposity, as we excluded children with BMI above 85th percentile for age and sex.

There is a known association between hypothyroidism and hyperlipidemia, and many individuals with DS have hypothyroidism; however, hypothyroidism requiring treatment was one of the exclusion criteria for this study. **Hill et al. (2013)** postulated that the excess mortality from cardiovascular disease (CVD) in DS may be related to unrecognized congenital heart defect, increased BMI, and tendancy toward diabetes mellitus in persons with DS. However, these conditions were excluded in our study, suggesting that an unfavorable lipid profile may also play a role in the increased CVD mortality of individuals with DS.

Given our study design and results, congenital heart defects, hypothyroidism, weight status, glucose, and insulin levels are unlikely to explain the difference in lipid profile in these children with DS compared to their normal children, and the question of whether over-expression of chromosome 21 directly influences lipid profile can be raised. In a study screening for additional familial combined hyperlipidemia genes, a locus conferring susceptibility to elevated apoB levels was identified on chromosome 21 **(Pajukanta et al., 2016)**.

In our study, we noted that there is no correlation between increasing age and different elements of lipid profile in the Down syndrome group, which may clarify that the difference in lipid profile may be genetically determined. This may go with the result of a study performed on fetuses with DS. It was suggestive of abnormalities of lipid metabolism in utero, before other factors could influence lipid levels. In that study, DS fetuses were also found to have increased TC and increased apolipoprotein A levels compared to the controls, it was concluded that fetuses with trisomy 21 have abnormalities of lipid metabolism that are specific and may be genetically determined **(Bocconi et al., 2017)**.

In a previous study, it was found that children with DS had increased leptin levels for percentage of body fat when compared with normal children, suggesting increased leptin resistance at the same fat level with DS **(Magge et al., 2018)**. Leptin is also significantly associated with total cholesterol and triglycerides, even after adjusting for BMI **(Sattar et al., 2016)**. Therefore, it is possible that increased leptin resistance in DS may play a role in the lipid profile of the children with DS observed in our study.

On the other hand, a study performed by **Tansley et al. (2014)** has produced some conflicting results. It was a pilot study performed to assess traditional serum sterol lipids and lipoproteins, as well as markers of sterol biosynthesis, metabolites, and plant sterols in 20 subjects with DS compared to age-matched controls. It was found that the levels of nearly all lipids and lipoproteins examined are similar to control subjects, suggesting that trisomy 21 does not lead to pronounced general alterations in sterol lipid metabolism.

The limitations of this study included a failure to control the blood sugar levels, insulin levels, or hemoglobin A1c in the study group which could have potentially affected lipid levels. With the increased life expectancy for individuals with DS and the increasing importance of adult chronic disease in this population, optimal cardiovascular disease prevention is necessary in children and adults with DS.

RECOMMENDATIONS

The conclusions of the present study are that:

- Down syndrome cases had values of triglyceride statistically higher than healthy children.
- DS had values of cholesterol statistically higher than healthy children.
- DS had values of low density lipoprotein statistically higher than healthy children.
- Healthy children had values of high density lipoprotein statistically higher than DS.
- It was found that there was no correlation between sex and different elements of lipid profile within Down syndrome group.
- There was no correlation between age and different elements of lipid profile within the two groups.

LIMITATION OF THE STUDY

The limitations of this study included a failure to control the blood sugar levels, insulin levels, or hemoglobin A1c in the study group which could have potentially affected lipid levels. With the increased life expectancy for individuals with DS and the increasing importance of adult chronic disease in this population, optimal cardiovascular disease prevention is necessary in children and adults with DS.

REFERENCES

1. **Adelekan T, Magge S, Shults J, Stallings V and Stettler N, (2012):** Lipid profiles of children with Down syndrome compared with their siblings. Pediatrics; 129(6): e1382-e1387.
2. **Bocconi L, Nava S, Fogliani R, Nicolini U, (2017):** Trisomy 21 is associated with hypercholesterolemia during intrauterine life. Am J Obstet Gynecol; 176: 540-3.
3. **Calefati J, (2009):** College is possible for students with intellectual disabilities, Us news and world report. Available at: http:\www.usnews.com.\education\articles\Collegeis-possible-for-students-with-intellectual–disabilities, 2013.
4. **Day SM, Strauss DJ, Shavelle RM, Reynolds RJ, (2015):** Mortality and causes of death in persons with Down syndrome in California. Dev Med Child Neurol; 47: 171-6.
5. **Dörner K, Gaethke AS, Tolksdorf M, (2010):** Cholesterol fractions and triglycerides in children and adults with Down's syndrome. Clin Chim Acta ; 142: 307-11.
6. **Glasson EJ, Sullivan SG, Hussain R, Petterson BA, Montgomery PD, (2012):** The changing survival profile of people with Down's syndrome: implications for genetic counselling. Clin Genet ; 62: 390-3.
7. **Grant G, Goward P, Ramcharan P, Richarelson M, (2010):** Life cycle approach to valuing people. ISBN; 978: 43-4.
8. **Hill DA, Gridley G, Cnattingius S, (2013):**

Mortality and cancer incidence among individuals with Down syndrome. Arch Intern Med; 163: 705-11.

9. **Magge SN, O'Neill KL, Shults J, Stallings VA, Stettler N, (2018):** Leptin levels among prepubertal children with Down syndrome compared with their siblings. J Pediatr ; 152: 321-6.

10. **Pajukanta P, Terwilliger JD, Perola M, (2016):** Genome wide scan for familial combined hyperlipidemia genes in Finnish families, suggesting multiple susceptibility loci influencing triglyceride, cholesterol, and apolipoprotein B levels. Am J Hum Genet; 64: 1453-63.

11. **Pueschel SM, Craig WY, Haddow JE, (2005):** Lipids and lipoproteins in persons with Down's syndrome. J Intellect Disabil Res ; 36: 365-9.

12. **Roizen NJ and Patterson D, (2013):** Down's syndrome, Lancet; 361: 1281-9.

13. **Sattar N, Wannamethee G, Sarwar N, (2016):** Leptin and coronary heart disease: prospective study and systematic review. J Am Coll Cardiol ; 53: 167-75.

14. **Tahira A, Sheela M, Justine S, Virginia S, Nicolas S, (2014):** Lipid Profiles of Children With Down Syndrome Compared With Their Siblings. http://pediatrics.aappublications.org/content/early/2012/.

15. **Tansley G, Daniel T, Lütjohann D,Head E, Wellington CL, (2014):** Sterol Lipid Metabolism in Down Syndrome Revisited: Down Syndrome Is Associated with a Selective Reduction in Serum Brassicasterol Levels. Available at: www.ncbi.Nlm.nih.gov/pubmed/22649448.