

Assessment of glucose levels and lipid profiles in adults with Down syndrome in Punjab (India)

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ABSTRACT

Down syndrome is the most common chromosomal abnormality and cause of mental retardation globally. Persons born with DS are at an increased risk for various health conditions, including thyroid disease, leukemia, congenital heart defects, gastrointestinal tract abnormalities, obesity and diabetes mellitus. The present case control study was conducted by taking blood samples on 420 subjects aged 20 to 40 years including 210 adults with down syndrome (120 males and 90 females) and 210 age and sex matched healthy controls (120 males and 90 females) from different areas of Punjab (India). The objectives of the study were to assess and compare the glucose levels and lipid profiles in adults with down syndrome and controls and to further evaluate the prevalence of hyperglycemia and dyslipidemia in both the groups. The levels of glucose, high-density lipoprotein (HDL), triglyceride (TG) and very low-density lipoprotein (VLDL) were higher in the males with down syndrome than their control peers with statistically significant differences. The values of total cholesterol and LDL were greater in controls with statistically significant differences for LDL. The values of glucose and all the variables of lipid profile were lesser in females with down syndrome than the controls with statistically non-significant differences except for LDL. Greater percentage of DS males had alterations in glucose levels in comparison to the controls while equal percentages of females were hyperglycaemic. The categorization on the basis of cholesterol levels showed that greater percentage of control subjects were in the risk category while the majority of DS subjects were having normal cholesterol values. According to the LDL levels, males (12.5% DS and 16.67% controls) and DS females (11.11%) were in high and very high risk category. On the basis of HDL values, greater percentage of males from both the groups were having normal levels while the females from both the groups were in lower risk category. Half of the sample of DS males was at borderline on the basis of triglyceride levels. Greater percentage of males (controls) was at the high risk level in comparison to their DS counterparts. A significant number of DS females (55.56%) were in the high risk category. The males of control group (54.17%) and DS females (66.67%) were having normal VLDL levels. Greater percentages of DS males were in the borderline and high risk category than their control peers.

Keywords: Down syndrome, controls, glucose, lipid profile, hyperglycaemic

INTRODUCTION

Down syndrome (DS) is one of the chromosomal abnormalities with numerous manifestations. The condition is the most common cause of mental retardation in the world (Pitetti *et al.*, 1992). Esquirol provided the first description of a child who presumably had Down syndrome (Shetty *et al.*, 2013). In 1959, Jerome Lejuene, a French physician identified Down syndrome as chromosomal abnormality. Lejeune and his co-workers (Lejeune *et al.*, 1959) demonstrated that the syndrome was a result of trisomy of chromosome 21. In 1974, Niebuhr suggested that the "Down syndrome phenotype" might be caused by the duplication of only a part of chromosome 21 band q22, which itself represents about one half of the long arm. More than 1 million people are suffering from Down syndrome in the world (Morris, 2008) which is recognizable at the time of birth because of the existence of some special attributes. The individuals suffering from DS have large body frame abnormalities and impaired brain development and functioning, which further lead to retarded intellectual development.

It has been estimated that the incidence of Down syndrome is 1 in 1000 to 1 in 1100 live births worldwide. Approximately 3000 to 5000 children are born with Down syndrome every year. Nearly 2, 50,000 families in United States of America are affected by this disorder. The recent incidence of Down syndrome is estimated at 4.6 per 10,000 births (Grant *et al.*, 2010). Persons born with DS are at an increased risk for various health conditions, including thyroid disease, leukemia, congenital heart defects, gastrointestinal tract abnormalities, obesity and diabetes mellitus (Roizen and Patterson, 2003). Myrelid *et al.* (2002) and Roizen (2002) have reported high prevalence of fatness and metabolic illnesses among young DS population. Glucose is the reducing monosaccharide that serves as the principal source of cellular energy in the body. It enters into the cell under the influence of insulin and undergoes a series of chemical reactions to produce energy. Lipid profile is a group of blood tests that serve as an initial broad medical screening tool for abnormalities in lipids, such as cholesterol and triglycerides. The results of this test can identify certain genetic diseases and can determine approximate risks for cardiovascular diseases, certain forms of pancreatitis, and other diseases. The lipid profile typically includes total cholesterol(TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides(TG) and very low-density lipoprotein (VLDL). Metabolic syndrome might be even more prevalent in adults with Down syndrome, as it has been frequently associated with an alteration in lipid profiles (Flore *et al.*, 2005). Adults with DS are more susceptible to obesity, diabetes and insulin resistance, but the

consequential risk of cardiovascular diseases remain controversial (Da la Garza-Hernandez *et al.*, 2016). Recent scientific advancements in research and diagnosis of DS and prevention of associated medical conditions have caused a significant increase in life expectancy in individuals with this disorder (Mazurek and Wyka, 2015). Increase in life expectancy and an elevated risk of obesity and diabetes mellitus in individuals with DS further raise concerns about long term health outcomes (Glasson *et al.*, 2002). Obesity and insulin resistance, which are common among individuals with DS are associated with unfavourable (more atherogenic) lipid profiles, characterized by high triglycerides and low HDL cholesterol levels. The objectives of the present study were to assess and compare the biochemical characteristics (blood glucose levels and lipid profile) in Down syndrome adults and controls (both sexes). Further the prevalence of risk of cardiovascular diseases according to increased levels of glucose and lipid components were evaluated in the subjects.

MATERIAL AND METHODS

The present study was a case control study conducted from 2013 to 2014 in the state of Punjab, India. Data on 420 subjects (20 to 40 years old) were collected which included 210 adults with down syndrome as cases (120 males and 90 females) and 210 healthy age matched individuals as controls (120 males and 90 females). The project was funded by the University Grants Commission, New Delhi and approved by the Institutional Ethical Committee of Punjabi University, Patiala. The sample was collected from different areas of Punjab. The sample for the adults with Down syndrome was collected from various institutions and households where such individuals resided. The pre-tested pre-designed questionnaire was used to assess the socio-demographic characteristics of the subjects. The study included patients whose legal guardians gave consent for their participation by agreeing and signing the consent form along with the controls who also gave their written consent. All the cases had their karyotypic analysis done, confirming trisomy 21. The blood sample for biochemical analysis was withdrawn by a trained technician and the tests for assessing lipid profile and glucose levels were performed in the laboratory of Department of Human Genetics, Punjabi University, Patiala. Statistical analysis was done by using the software SPSS 16. Student's t-test was used to compare the variables of the two studied groups.

RESULTS

The mean glucose value of the males with Down syndrome was $142.67 \text{ mg/dl} \pm 55.97$ and that of controls was $109.41 \text{ mg/dl} \pm 27.45$ (Table 1). The mean total cholesterol value of the

males with Down syndrome was 161.26 mg/dl \pm 37.59 and that of controls was 181.27 mg/dl \pm 65.53. The mean HDL value of the DS males was 57.67 mg/dl \pm 12.92 and that of controls was 42.30 mg/dl \pm 12.13. Similarly the mean LDL value of the males with Down syndrome was 69.32 mg/dl and that of controls was 113.81 mg/dl. The mean triglyceride value of the DS males was 171.35 mg/dl \pm 79.35 and that of controls was 125.79 mg/dl \pm 64.38. The mean VLDL values of the males with Down syndrome was 34.27 mg/dl \pm 15.87 and that of controls was 25.16mg/dl \pm 12.87. In the males with Down syndrome, the levels of glucose, HDL, triglycerides and VLDL were higher than their control peers with statistically significant differences. The values of total cholesterol and LDL were greater in controls with statistically significant differences for LDL.

Table 1. Descriptive statistics of glucose and lipid profile of males

Variable	Cases (N = 120)			Controls (N = 120)			t- value
	Mean	SD	SEM	Mean	SD	SEM	
Glucose (mg/dl)	142.67	55.97	12.21	109.41	27.45	5.99	2.44*
Total cholesterol (TC) (mg/dl)	161.26	37.59	8.20	181.27	65.53	14.30	1.20
HDL (mg/dl)	57.67	12.92	2.82	42.30	12.13	3.03	3.67***
LDL (mg/dl)	69.32	29.20	6.37	113.81	57.57	12.54	3.37**
Triglyceride (mg/dl)	171.35	79.35	17.31	125.79	64.38	14.05	2.04*
VLDL (mg/dl)	34.27	15.87	3.46	25.16	12.87	2.81	2.04*

* Statistically significant $p < 0.05$

** Statistically significant $p < 0.01$

*** Statistically significant $p < 0.001$

The mean glucose value of the females with Down syndrome was 107.13 mg/dl \pm 39.92 and that of controls was 115.67 mg/dl \pm 28.30 (Table 2). The mean total cholesterol value of the females with Down syndrome was 138.29 mg/dl \pm 38.25 and that of controls was 170.80 mg/dl \pm 55.56. The mean HDL value of the DS females was 55.43 mg/dl \pm 16.48 and that of controls was 55.75 mg/dl \pm 15.70. Similarly the mean LDL value of the females with Down syndrome was 60.14 mg/dl and that of controls was 91.13 mg/dl. The mean triglyceride value of the DS females was 113.61 mg/dl \pm 62.31 and that of controls was 119.59 mg/dl \pm 49.66. The mean VLDL value of the females with Down syndrome was 22.72 mg/dl \pm 14.35 and that of controls was 23.92 mg/dl \pm 9.93. The values of glucose and all variables of lipid

profile were lesser in females with Down syndrome than the controls with statistically non-significant differences except for LDL.

Table 2. Descriptive statistics of glucose and lipid profile of females

Variable	Cases (N = 90)			Controls (N = 90)			t- value
	Mean	SD	SEM	Mean	SD	SEM	
Glucose (mg/dl)	107.13	32.92	11.64	115.67	28.30	9.43	0.57
Total cholesterol (TC) (mg/dl)	138.29	38.25	12.75	170.80	55.56	18.52	1.15
HDL (mg/dl)	55.43	16.48	5.49	55.75	15.70	5.23	0.04
LDL (mg/dl)	60.14	15.73	5.24	91.13	29.84	9.94	3.10**
Triglyceride (mg/dl)	113.61	62.31	20.77	119.59	49.66	16.55	0.22
VLDL (mg/dl)	22.72	14.35	4.78	23.92	9.93	3.31	0.45

* Statistically significant $p < 0.05$

** Statistically significant $p < 0.01$

*** Statistically significant $p < 0.001$

Assessment of hyperglycemia was done in the cases and controls on the basis of criteria given by Kirschner and Woods (2001) (Table 3). In males with Down syndrome, 25% of the individuals were normal and 75% were hyperglycaemic; while in males of control group, 45.83% were normal and 54.17% hyperglycaemic. In the females with Down syndrome, 44.44% and 55.56% were normal and hyperglycaemic respectively. A similar ratio was observed in females of control group too.

Table 3. Categorization of the subjects on the basis of blood glucose levels

Glucose levels	Males		Females	
	Cases (N = 120)	Controls (N = 120)	Cases (N = 90)	Controls (N = 90)
Normal ≤ 110	30(25%)	55(45.83%)	40(44.44%)	40(44.44%)
Hyperglycemia >110	90(75%)	65(54.17%)	50(55.56%)	50(55.56%)

The subjects of the present study were categorized to be in normal, borderline, risk or high risk category according to levels of different components of lipid profile according to the criteria of National Cholesterol Program NCEP ATP III (2002).

Table 4. Categorization of the subjects on the basis of cholesterol

Cholesterol levels	Males		Females	
	Cases (N = 120)	Controls (N = 120)	Cases (N = 90)	Controls (N = 90)
Normal <200	95(79.17%)	80(66.67%)	90(100%)	80(88.89%)
Borderline 200-239	25(20.83%)	25(20.83%)	-	10(11.11%)
High risk >240	-	15(12.5%)	-	-

On the categorization of the males of both the groups on the basis of cholesterol values(National Cholesterol Program NCEP ATP III, 2002), it was observed that there were 79.17% normal, 20.83% at border line and no one was at the risk in males with down syndrome and in case of controls there were 66.67% normal, 20.83% at border line and 12.5% at high risk (Table 4). All the DS females were normal. In the control group, there were 88.89% normal and 11.11% at border line of risk of cardiovascular diseases.

Table 5. Categorization of the subjects on the basis of low-density lipoprotein (LDL)

Low-density lipoprotein (LDL) levels	Males		Females	
	Cases (N = 120)	Controls (N = 120)	Cases (N = 90)	Controls (N = 90)
Optimal <100	65(54.17%)	45(37.5%)	40(44.44%)	40(44.44%)
Sub Optimal 100-129	30(25%)	15(12.5%)	40(44.45%)	30(33.33%)
Borderline 130-159	10(8.33%)	25(20.83%)	-	20(22.22%)
High 160-189	15(12.5%)	20(16.67%)	10(11.11%)	-
Very high >190	-	15(12.5%)	-	-

There were 54.17% at optimal, 25% at sub optimal, 8.33% at border line, 12.5% at high risk and there was no male at very high risk in case of DS males for values of LDL (Table 5). Similarly in case of controls 37.5% were at optimal, 12.5% at sub optimal, 20.83% at border line, 16.67% at high risk and 12.5% at very high risk in case of controls respectively. The

LDL analysis showed that 44.44% were at optimal, 44.45% at sub optimal, 11.11% at high risk and there were no females at borderline and very high risk categories in case of DS females. Similarly in case of controls, there were 44.44% at optimal, 33.33% at sub optimal and 22.22% at border line.

The categorization for lower and higher risk on the basis of HDL values reported that 4.17% were at lower risk, 41.67% at the high risk and 54.17% were normal in case of males with down syndrome and in case of controls 29.17% were at lower risk, 8.33% at high risk and 62.5% were normal respectively (Table 6). On the basis of HDL, 88.89% were at lower risk, no one at high risk and 11.11% were normal in case of females with down syndrome and their control counterparts.

Table 6. Categorization of the subjects on the basis of high-density lipoprotein (HDL)

High-density lipoprotein (HDL) levels	Males		Females	
	Cases (N = 120)	Controls (N = 120)	Cases (N = 90)	Controls (N = 90)
Low <40	5(4.17%)	35(29.17%)	80(88.89%)	80(88.89%)
High ≥60	50(41.67%)	10(8.33%)	-	-
Normal 41-59	65(54.17%)	75(62.5%)	10(11.11%)	10(11.11%)

Table 7. Categorization of the subjects on the basis of triglycerides

Triglycerides levels	Males		Females	
	Cases (N = 120)	Controls (N = 120)	Cases (N = 90)	Controls (N = 90)
Normal <150	55(45.83%)	75(62.5%)	40(44.44%)	60(66.67%)
Borderline 150-199	60(50%)	30(25%)	-	20(22.22%)
High risk 200-499	5(4.17%)	15(12.5%)	50(55.56%)	10(11.11%)

There were 45.83% normal, 50% at border line and 4.17% at the high risk in case of males with down syndrome and in case of controls there were 62.5% normal, 25% at border line and 12.5% at high risk on the basis of triglyceride levels (Table 7). In DS females, 44.44%

were normal and 55.56% were at the high risk and in case of controls there were 66.67% normal, 22.22% at border line and 11.11% at high risk.

There were 33.33% normal, 33.33% at border line and 33.34% at the high risk in case of DS males and in controls there were 54.17% normal, 16.67% at border line and 29.16% were at high risk respectively for the VLDL levels (Table 8). In DS females, 66.67% were normal, 22.22% at border line and 11.11% at high risk and in case of controls there were 55.56% normal, 33.33% at border line and 11.11% at high risk respectively.

Table 8. Categorization of the subjects on the basis of very low-density lipoprotein (VLDL)

Very Low-density lipoprotein (VLDL) levels	Males		Females	
	Cases (N = 120)	Controls (N = 120)	Cases (N = 90)	Controls (N = 90)
Normal <25	40(33.33%)	65(54.17%)	60(66.67%)	50(55.56%)
Borderline 25-35	40(33.33%)	20(16.67%)	20(22.22%)	30(33.33%)
High >35	40(33.34%)	35(29.16%)	10(11.11%)	10(11.11%)

DISCUSSION

In the males with down syndrome, the levels of glucose, high-density lipoprotein (HDL), triglyceride (TG) and very low-density lipoprotein (VLDL) were higher than their control peers with statistically significant differences. The values of total cholesterol and LDL were greater in controls with statistically significant differences for LDL. The values of glucose and all the variables of lipid profile were lesser in females with down syndrome than their control peers with statistically non-significant differences except for LDL.

The results of the present study showed greater glucose levels in DS males than their control counterparts and lesser glucose levels in DS females than their control peers. Greater percentage of DS subjects were hyperglycaemic. Da la Garza-Hernandez *et al.* (2016) reported glucose alterations in 11.42% of DS subjects. It was also observed by van de Louw *et al.* (2009) that the women with DS had lower fasting plasma glucose than those of women with intellectual disability. Al-Awadi *et al.* (2001) observed that Kuwaiti DS adolescents had disturbed glucose levels. The results are in conformity with the ones reported by Da la Garza-Hernandez *et al.* in Mexican DS population (2016).

The present study revealed that the total cholesterol of DS subjects (both sexes) was lesser as compared to that of controls with statistically non-significant differences. The categorization on the basis of cholesterol levels showed that greater percentage of control subjects were in the risk category while the majority of DS subjects were having normal values. AL-Awadi *et al.* (2001) reported low lipids in Kuwaiti DS adolescents. In agreement with the present results, Nishada *et al.* (1977), Salo *et al.* (1979), Dorner *et al.* (1984) and Tansley *et al.* (2012) reported that the patient's total cholesterol did not differ much from that of controls. Zamorano *et al.* (1991) in Chile, AL-Awadi *et al.* (2001), Zigman *et al.* (2008), Adelekan *et al.* (2012), Salih *et al.* (2015) in Sudan and Da la Garza-Hernandez *et al.* (2016) concluded that the individuals with Down syndrome had significantly higher values of total cholesterol than their control counterparts. Non significant differences were reported for total cholesterol between cases and controls by Pueschel *et al.* (1992). Moustafa *et al.* (2015) concluded that the values of cholesterol were more in controls as compared to DS subjects. The results of the present study are in conformity with the earlier studies by Pueschel *et al.* (1992) and Moustafa *et al.* (2015).

The male subjects with Down syndrome had greater concentration of HDL as compared to that of controls and the differences between the two groups were statistically significant while the HDL levels were almost similar in females of both the groups. On the basis of HDL, greater percentage of males from both the groups were having normal levels while the females from both the groups were having the levels in lower risk category. Decreased HDL levels were observed by Da la Garza-Hernandez *et al.* (2016) in 2.09% of DS subjects. On the other hand, Adelekan *et al.* (2012) reported that the children with Down syndrome had lower concentration of HDL than their siblings. Zamorano *et al.* (1991) and Pueschel *et al.* (1992) also reported that children with Down syndrome have a constant deficit of HDL. Salih *et al.* (2015) reported statistically lower HDL levels in adults with DS than their control peers. Tansley *et al.* (2012) observed non significant differences for HDL among controls and DS subjects. The results of the present study are in conformity with those reported by Tansley *et al.* (2012).

The values of LDL in controls were higher than that of cases (in both the sexes). The differences in the two groups were statistically significant in males as well as in females. According to the LDL levels, it was observed that to a large extent, the subjects of the present study were in the first three categories. Out of the total sample, males (12.5% DS and 16.67% controls) and DS females (11.11%) were in high and very high risk category. Zamorano *et al.*

(1991) Adelekan *et al.* (2012) Salih *et al.* (2015) and Da la Garza-Hernandez *et al.* (2016) (in 73.42% of total DS individuals) reported that the concentration of LDL was statistically higher in the individuals with Down syndrome than that of controls. Pueschel *et al.* (1992) concluded that the differences for LDL were non-significant among the Down syndrome individuals and controls. The results of the present study are not in agreement with the results reported earlier by other investigators.

The males with Down syndrome had greater concentration of triglycerides than that of controls. The differences in the two groups were statistically significant, while the females (DS) had lesser values than their control counterparts. Half of the sample of DS males was at borderline on the basis of triglyceride levels. Greater percentage of males of control group were at the high risk level in comparison to their DS counterparts. A significant number of DS females (55.56%) were in the high risk category. The results are in conformity with the earlier studies by Nishada *et al.* (1977), Salo *et al.* (1979), Pueschel *et al.* (1992), Zamorano *et al.* (1991), Adelekan *et al.* (2012), Salih *et al.* (2015) and Da la Garza-Hernandez *et al.* (2016) who have concluded that the individuals with Down syndrome had statistically significant increase in triglyceride levels than that of controls. Whereas AL-Awadi *et al.* (2001) and Moustafa *et al.* (2015) reported that the individuals with Down syndrome had lower values of triglycerides than their control counterparts.

The values of VLDL in males with down syndrome were higher than that of controls and lesser than controls in DS females. The differences between the two groups were statistically significant in males and non-significant in the females. The males of control group (54.17%) and DS females (66.67%) were having normal VLDL levels. Greater percentages of DS males were in the borderline and high risk category than their control peers. Salo *et al.* (1979) reported that the concentration of VLDL was higher in DS subjects than that of controls. The results of the present study are in agreement with the earlier investigated report.

The present study found abnormal lipid profile in the subjects above the age of 20 years, suggesting that it is necessary to make a screening in adult patients. Greater prevalence of dyslipidemia was reported with elevated LDL levels, whereas DS was earlier reported to be an 'atheroma free model' (Murdoch *et al.*, 1977). The difference in lipid profile levels in DS subjects than the controls cannot be explained. There is a possibility that the over-expression of chromosome 21 might be influencing the increase in levels of lipid components. Pajukanta *et al.* (1999) screened additional familial combined hyperlipidemia genes and identified a locus on chromosome 21 which was responsible for conferring susceptibility to elevated apo

B levels. It is further required to conduct longitudinal studies of Down syndrome subjects to determine whether these differences in lipid profile played a role to increase morbidity and mortality from cardiovascular diseases. This study was the first of its kind in Punjab (India) in which the lipid profile and glucose levels were estimated in adults with Down syndrome.

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