

# Glycaemic Control and Dyslipidemia among patients with type 1 diabetes mellitus in diabetes center Al-Baha region, Saudi Arabia

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## Abstract

**Background:** Dyslipidemia is very common in patients with type 1 diabetes mellitus. Dyslipidemia is a substantial risk factor for having cardiovascular disease (CVD) and is associated with higher percentages of morbidity and mortality in patients with type 1 DM. Several studies have shown that poor glycaemic control (PGC) and high level of glycated haemoglobin A1c (HbA1c) in patients with T1DM are associated with lipid peroxidation and oxidative stress, both of which contribute to atherosclerosis.

**Aim:** To assess Glycaemic Control and Dyslipidemia in type 1 diabetic patients in diabetic center Al-Baha region, Saudi Arabia.

**Methodology:** A record based descriptive cross sectional study was conducted at diabetes center in Al-Baha region, located in the southern area of Saudi Arabia. The study was conducted by reviewing medical files of type 1 diabetic children during the period from 15th of December 2020 to 1st of March 2021. Recently diagnosed type 1 diabetic cases (< 3 months), and those with missing data were excluded. Files fulfilling the inclusion criteria were included using systematic random sampling technique by selecting each 3rd file. The data extracted included child personal data including age and gender, child duration of diabetes, diabetes control by measuring HbA1c, and laboratory investigations including lipid profile.

**Results:** The study included 225 children with type 1 DM. Children's ages ranged from 1 to 21 years with mean age of  $10.4 \pm 3.5$  years old. Exact of 120 (53.3%) diabetic children were males. The majority of the diabetic children had the disease for 1-4 years (63.6%; 143). Exactly 132 (58.7%) children had hypercholesterolemia with average cholesterol level of  $.5 \pm 0.95$  mmol/ L. As for LDL level, it was abnormal among 9 (4%) diabetic children with average level of  $2.74 \pm 0.91$  mmol/L. Exactly 12 (5.3%) children had abnormal TG level with average level of  $1.55 \pm 0.51$  mmol/L. HDL was below normal among 17 (7.6%) children with average level of  $1.46 \pm 0.40$  mmol/L. Exactly 69.2% of diabetic children aged 10 years or more had dyslipidemia compared to 50.6% of those who were below the age of 20 years with recorded statistical significance ( $P=.006$ ).

**Conclusions:** In conclusion, the current study revealed that dyslipidemia is a common finding among diabetic cases including type 1 diabetes mellitus. Also, there is a significant association between glycaemic control and having abnormal lipid profile especially for cholesterol and HDL.

**Key words:** Dyslipidemia, type 1 DM, lipid profile, glycaemic control, IDDM, relations

## Background

Type-1 diabetes (T1D), previously known as Juvenile Diabetes is an autoimmune disease with genetic background in its pathology, featured by damage of pancreatic  $\beta$ -cells, causing absolute insulin deficiency [1, 2]. Insulin is a hormone required for the body to use blood sugar. Before treatment this results in high blood sugar levels in the body [3, 4]. Worldwide, nearly 425 million adults (20–79 years) had diabetes in 2017, with about 5% to 10% diagnosed with T1D [5]. The major causes of morbidity and mortality in patients with T1D are attributed to diabetes complications. Intensive insulin therapy showed a significant role in preventing progression of diabetes-related complications, thus resulting in good glycaemic control [6].

Among the leading causes of death in patients with diabetes, are atherosclerotic complications [7]. Therefore, it is crucial to detect risk factors, including lipid profile, which explains their cardiovascular risk. The lipid profile of patients with type 1 diabetes mellitus is mainly affected by their glycaemic control. Cases with poorly controlled type 1 diabetes had high levels of total triglyceride and total cholesterol with varying levels of high-density lipoprotein cholesterol (HDL-C) [8-10].

Glycaemic control, as expressed by mean blood glucose concentrations and percentage of glycated haemoglobin, is significantly amended with the introduction of insulin infusion pumps compared with the non-optimized insulin injection therapy that was dominant in management of diabetes until a relatively few years ago [11, 12]. However, unlike type 2 diabetes, epidemiological data on the prevalence of dyslipidemia and phenotype distribution in type 1 diabetes mellitus are scarce and are mostly based on total triglyceride and total cholesterol concentrations alone [13]. However, glycaemic control is a vital modifiable risk factor that affects the progressive rate of diabetic complications. Though, hypoglycemia is a serious worry for diabetic patients, and fear of hypoglycemia can negatively affect the acceptance of insulin therapy and the capability to lower HbA1c levels effectively through intensive treatment [14].

Also, the lipid profile of patients with type 1 diabetes mellitus depends mainly on glycaemic control. Patients with poorly controlled T1D reported high levels of total triglyceride and total cholesterol and variable concentrations of high-density lipoprotein cholesterol [15-18]. The current study aimed to assess prevalence and determinants of dyslipidemia, glycaemic control and dyslipidemia in type 1 diabetic patients in a diabetic center Al-Baha region, Saudi Arabia.

## Methodology

A record based descriptive cross sectional study was conducted at diabetes center in Al-Baha region, located in the southern area of Saudi Arabia. It has an area of 9,921 km<sup>2</sup>, and a population of 476,172 (2017). Its capital is Al-Baha [19]. The study was conducted by reviewing medical files of type 1 diabetic children during the period from 15th of December 2020 to 1st of March 2021. Type 1 diabetic patients, including those who are using insulin pump, who had regular follow-up at diabetic center, and their I file had complete data were included. Recently diagnosed type 1 diabetic cases (< 3 months), and those with missing data were excluded. Files fulfilling the inclusion criteria were included using systematic random sampling technique by selecting each 3rd file and were then reviewed for data extraction using pre-structured data extraction sheet to avoid error and minimize interrater bias. The data extracted included child personal data including age and gender, child's duration of diabetes, diabetes control by measuring HbA1c, and laboratory investigations including lipid profile.

## Dyslipidemia

According to American Diabetes Association (ADA), [20] dyslipidemia was defined as having hypercholesterolemia and hypertriglyceridemia (LDL-C >4.13 mmol/L [>160 mg/dL] and triglyceride >2.25 mmol/L [>200 mg/dL], respectively), Low HDL-C concentrations were less than 0.9 mmol/L (<35 mg/dL) for men and less than 1.1 mmol/L (<45 mg/dL) for women and dyslipidemia was considered present if one or more of these lipid or lipoprotein levels are abnormal [21, 22].

## Data Analysis

After data were collected, it was modified, coded and entered into statistical software IBM SPSS version 22 (SPSS, Inc. Chicago, IL). All statistical analysis was done using two tailed tests. P value less than 0.05 was considered to be statistically significant. Descriptive analysis based on frequency and percentage distribution was done for all variables including demographic data, diabetes data, and laboratory findings. Cross tabulation was used to test for the distribution of dyslipidemia by children's bio-demographic data. Pearson chi-square test was used to test for relations significance. Exact tests were used to assess significant association between dyslipidemia and diabetic children lipid profile.

## Results

The study included 225 children with type 1 DM. Children's ages ranged from 1 to 21 years with mean age of 10.4  $\pm$  3.5 years old. Exactly 120 (53.3%) diabetic children were males. The majority of the diabetic children had the disease for 1-4 years (63.6%; 143) and 31 (13.8%) had the disease for less than 1 year. As for diabetic control, it was poorly controlled among 148 (65.8%) of the children while 9 children (4%) had good diabetic control (Table 1).

**Table 1: Personal data of type 1 diabetic children, Al-Baha, Saudi Arabia**

Personal data	No	%
<b>Age in years</b>		
< 10 years	79	35.1%
> 10 years	146	64.9%
<b>Gender</b>		
Male	120	53.3%
Female	105	46.7%
<b>DM duration in years</b>		
< 1 year	31	13.8%
1-4	143	63.6%
5-9	51	22.7%
<b>Diabetic control (HA1c)</b>		
Good	9	4.0%
Fair	68	30.2%
Poor	148	65.8%

Table 2 shows lipid profile among type 1 Diabetic children. Exactly 132 (58.7%) children had hypercholesterolemia with average cholesterol level of  $4.5 \pm 0.95$  mmol/ L. As for LDL level, it was abnormal among 9 (4%) diabetic children with average level of  $2.74 \pm 0.91$  mmol/L. Exactly 12 (5.3%) children had abnormal TG level with average level of  $1.55 \pm 0.51$  mmol/L. HDL was below normal among 17 (7.6%) children with average level of  $1.46 \pm 0.40$  mmol/L. Totally, dyslipidemia was detected among 141 (62.7%) of the included diabetic children with type 1 DM (Figure 1).

**Table 2: Lipid profile among type 1 Diabetic children, Al-Baha, Saudi Arabia**

Lipid profile	No	%	Mean $\pm$ SD
<b>Hypercholesterolemia</b>			
Normal	93	41.3%	$4.5 \pm 0.95$ mmol/ L
Abnormal	132	58.7%	
<b>HDL</b>			
Normal	208	92.4%	$1.46 \pm 0.40$ mmol/L
Abnormal	17	7.6%	
<b>LDL level</b>			
Normal	216	96.0%	$2.74 \pm 0.91$ mmol/L
Abnormal	9	4.0%	
<b>Hypertriglyceridemia</b>			
Normal	213	94.7%	$1.55 \pm 0.51$ mmol/L
Abnormal	12	5.3%	

Figure 1: Prevalence of dyslipidemia among children with type 1 DM, Al-Baha, Saudi Arabia

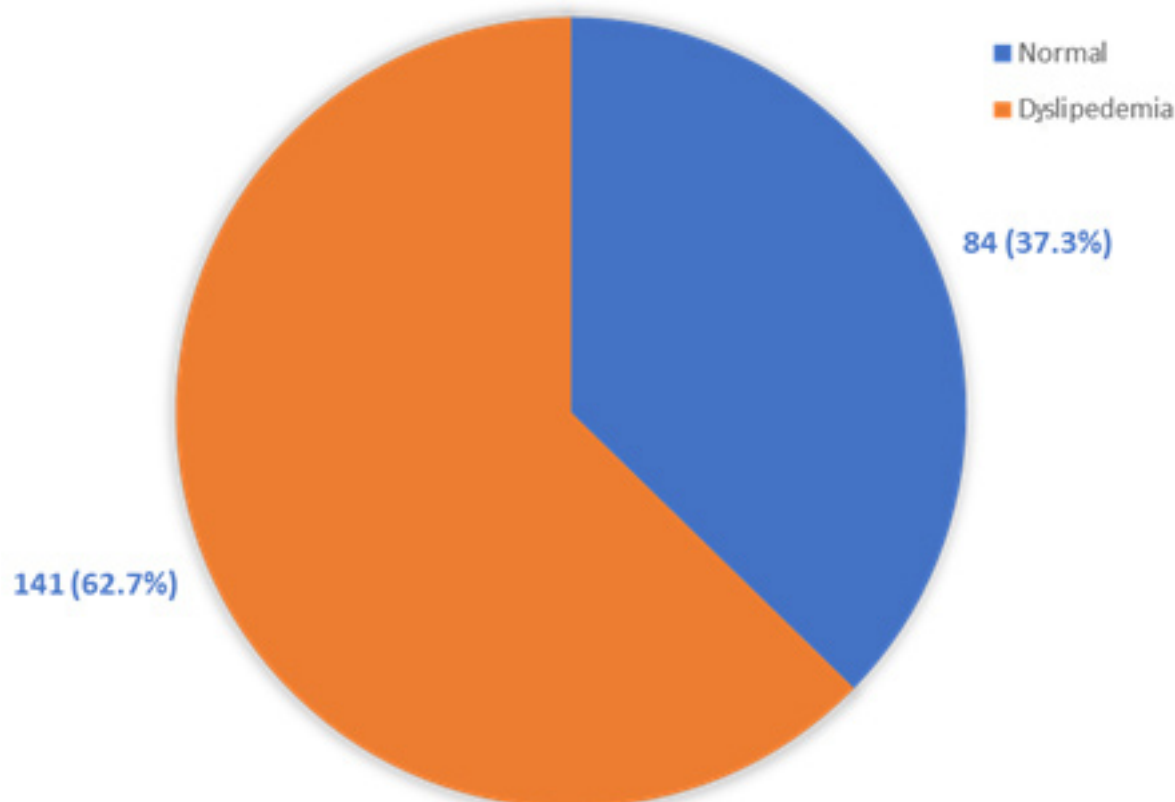


Table 3. Distribution of dyslipidemia among children with type 1 DM, Al-Baha, Saudi Arabia

Personal data	Dyslipidemia				P-value
	Normal		Dyslipidemia		
	No	%	No	%	
<b>Age in years</b>					
< 10 years	39	49.4%	40	50.6%	.006*
> 10 years	45	30.8%	101	69.2%	
<b>Gender</b>					
Male	44	36.7%	76	63.3%	.825
Female	40	38.1%	65	61.9%	
<b>DM duration in years</b>					
< 1 year	12	38.7%	19	61.3%	.134
1-4	59	41.3%	84	58.7%	
5-9	13	25.5%	38	74.5%	
<b>Diabetic control</b>					
Good	6	66.7%	3	33.3%	.048*
Fair	29	42.6%	39	57.4%	
Poor	49	33.1%	99	66.9%	

P: Pearson X2 test

\* P &lt; 0.05 (significant)

Table 3 illustrates distribution of dyslipidemia among children with type 1 DM. Exactly 69.2% of diabetic children aged 10 years or more had dyslipidemia compared to 50.6% of those who were below the age of 20 years with recorded statistical significance (P=.006). Also, 66.9% of children with poor diabetic control had dyslipidemia in comparison to 33.3% of those with good diabetes control (P=.048). Diabetic child gender and duration of diabetes were insignificantly associated with dyslipidaemia.

**Table 4. Distribution of lipid profile according to dyslipidemia among type 1 diabetic children**

Lipid profile	Dyslipidemia				P-value
	Normal		Dyslipidemia		
	No	%	No	%	
<b>Hypercholesterolemia</b>					
Normal	84	100.0%	9	6.4%	.001*
Abnormal	0	0.0%	132	93.6%	
<b>HDL</b>					
Normal	84	100.0%	124	87.9%	.001*
Abnormal	0	0.0%	17	12.1%	
<b>LDL level</b>					
Normal	84	100.0%	132	93.6%	.018*
Abnormal	0	0.0%	9	6.4%	
<b>Hypertriglyceridemia</b>					
Normal	84	100.0%	129	91.5%	.006*
Abnormal	0	0.0%	12	8.5%	

P: Exact probability test

\* P < 0.05 (significant)

Regarding distribution of lipid profile according to dyslipidemia among type 1 diabetic children (Table 4), it was noticed that 93.6% of children with dyslipidemia had abnormal cholesterol level, 12.1% had abnormal HDL level, 6.4% had abnormal LDL level, and 8.5% had abnormal TG level, all with recorded statistical significance (P < 0.05).

**Table 5. Distribution of lipid profile according to glycaemic control among type 1 diabetic children**

Lipid profile	Diabetic control				OR (95% CI)
	Poor		Fair/ good		
	No	%	No	%	
<b>Hypercholesterolemia</b>					
Normal	57	38.5%	36	46.8%	1.4 (1.0-2.4) *
Abnormal	91	61.5%	41	53.2%	
<b>HDL</b>					
Normal	134	90.5%	74	96.1%	2.6 (0.9-9.3) *
Abnormal	14	9.5%	3	3.9%	
<b>LDL level</b>					
Normal	144	97.3%	72	93.5%	0.4 (0.10-1.5)
Abnormal	4	2.7%	5	6.5%	
<b>Hypertriglyceridemia</b>					
Normal	138	93.2%	75	97.4%	2.7 (0.58-12.7)
Abnormal	10	6.8%	2	2.6%	

\* P < 0.05 (significant)

Table 5 shows distribution of lipid profile according to glycaemic control among type 1 diabetic children. Children with poor diabetic control recorded 1.5 times more likelihood for hypercholesterolemia compared to those with good control (OR: 1.4; 95% CI: 1.0-2.4). Also, those with poor glycaemic control had 2.6 times more likelihood for abnormal HDL level compared to others with good control (OR: 2.6; 95% CI: 0.9-9.3). No significant relation between glycaemic control and LDL or TG level was reported.



## Discussion

The current study aimed to assess dyslipidemia and its relationship with glycaemic control among type 1 diabetic children. Children with type 1 diabetes are susceptible for many other systemic disorders due to lipid profile changes including cardiovascular disease (CVD) [23-25]. The American Heart Association classifies type 1 diabetic children in the highest level for cardiovascular risk and proposes lifestyle modification besides pharmacological therapy for those with high cholesterol levels [26, 27]. Also, Global IDF/ISPAD Guideline, 2014 advocated checking for fasting blood lipids for diabetes in Childhood and Adolescents for diabetes duration exceeding 10 years. In cases of positive family history of hypercholesterolaemia, CVD, screening should start at age 2 years. If results are normal, screening should be repeated every 5 years [28]. In the current study, two thirds of the children (62.7%) had dyslipidemia where cholesterol was the highest reported lipid profile as more than half of the diabetic children had high cholesterol level (above normal). Other lipid profiles were not high among a significant portion of the children mainly LDL and triglycerides which were high among 4% and 5.3%, respectively. Dyslipidemia was significantly higher among diabetic children aged more than 10 years. The surprising finding was that it was not significantly associated with diabetes duration, but it was insignificantly higher among children who had type 1 diabetes for 5-9 years than those who were recently diagnosed (less than one year). Dyslipidemia was also significantly associated with all lipid profiles especially cholesterol level and HDL. These findings were consistent with Mona HM et al, [29] results who reported that 65% of type 1 diabetic children had dyslipidemia compared to 28% of non-diabetic control group. Also, the current study agreed with Rahma et al, [30] who found that 66% of the children with type 1 diabetes were dyslipidemic compared to 34% of the control group. Also, the current study findings were similar to others conducted by Wiltshire et al, [31] and Patiakas et al [32].

Regarding relation between dyslipidemia and diabetic control, the current study revealed that more than two thirds of the diabetic children with poor diabetic control were dyslipidemic compared to nearly half of those with fair control and only one third of those with good diabetic control. Also, the study revealed that poor diabetic control was associated with significantly more than doubled risk to have abnormal level of HDL and 40% more risk for having hypercholesterolemia. No significant relation between poor glycaemic control and LDL and TG level were detected in the current study. This may be somewhat confusing as in poorly controlled type 1 diabetes and even ketoacidosis, cases mostly have hypertriglyceridemia and reduced HDL [33]. Among type 1 diabetic patients, even with good glycaemic control, qualitative and functional abnormalities of lipoproteins are reported that are possibly atherogenic. These lipid profile abnormalities are risk factors for developing CV diseases. Though the mechanisms underlying type 1 diabetes associated dyslipidemia stay vague, the subcutaneous route of insulin administration, that is responsible for peripheral hyperinsulinemia, is

likely to be an important factor [34, 35]. Mostofizadeh N et al, [36] found that hypercholesterolemia was the most reported dyslipidemia in 29.1% of diabetic children with optimal glycaemic control (OGC) compared to 39.1% of others with poor glycaemic control (PGC). Abnormal level of low-density lipoprotein was significantly higher in cases with PGC than those with OGC. Also, the magnitude of hypercholesterolemia, hypertriglyceridemia, and low levels of high-density lipoprotein were higher in the PGC group but did not reach the significant threshold. There are many literature studies which assured the significant association between glycaemic control (level of HbA1c) and abnormal lipid profile among diabetic patients, but the main uncertainty was for the thresholds of HbA1c beyond which lipid levels begin to change [37-40].

Optimal glycaemic control is significantly associated with improved lipid profile and associated co-morbidities with better survival in patients with type 1 diabetes, leading to advanced changes in the causes of mortality, especially cardiovascular disease [41, 42].

## Conclusions and recommendations

In conclusion, the current study revealed that dyslipidemia is a common finding among diabetic cases including type 1 diabetes mellitus. Also, there is a significant association between glycaemic control and having abnormal lipid profile especially for cholesterol and HDL. Dyslipidemia was higher among children aged 10 years but not related to diabetes duration. Periodic screening for lipid profile among diabetic children is vital to help in early assessment of any abnormality and applying the appropriate intervention including health education for lifestyle and dietary habits which improves glycaemic control. Large scale studies are recommended to better understand the mechanism and pathogenesis of dyslipidemia and to assess the efficacy of good glycaemic control on improving rates of lipid abnormalities.

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