International Invention of Scientific Journal
Online ISSN: 2457-0958
Available Online at https://iisj.in **Volume 8, Issue 04 (October-November-December)|2024**|Page: 894-902
Original Research Paper-Medical Sciences

Investigation of lipid profile in type 1 diabetic children Referred to Ali Asghar Zahedan clinic in the year 1402-3

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Article Received: 01-October-2024, Revised: 21-October-2024, Accepted: 11-November-2024

ABSTRACT:
Introduction: According to the recommendations made, it seems necessary to check serum lipids in all type 1 diabetic patients, regardless of the length of time that has passed since the disease, and it emphasizes the accurate control of blood sugar using more appropriate patterns of insulin therapy. Also, considering the few studies conducted in the adolescent age group and type 1 diabetes. It is necessary to implement a low-cost follow-up program. Therefore, considering the importance of type 1 diabetes and the impact that this disease has on the individual, family and society, and pointing out that the level of lipid profile in young people with type 1 diabetes is variable, we decided to conduct a study to investigate the level of lipid profile in Type one debate people do. **Materials and methods**: In this descriptive-cross-sectional study, 52 type 1 diabetes patients who visited Ali Asghar Zahedan Hospital were selected using the non-probability sampling method and were examined in terms of their lipid profile. Patients with a history of hypothyroid disease, cholestasis, familial hypercholesterolemia, nephrotic syndrome, CRF, or receiving isoniazid, BB, estrogen, and clozapine drugs were excluded from the study. **Results**: 52 children with type 1 diabetes in the age range of 1 to 18 years were investigated. In terms of gender distribution, 29 of the children (55.8%) were boys and 23 of them (44.2%) were girls. There was no significant difference in lipid profile between boys and girls ($p>0.05$). Also, the average HbA1C ($P=0.069$), cholesterol ($P=0.07$) and HDL ($P=0.35$) did not differ significantly according to age, but the variables of triglyceride ($P=0.033$) and LDL ($P=0.01$) in children over 10 years old. It was more than children under 10 years old. **Conclusion**: Finally, it can be stated that the amount of lipid profile in type 1 diabetic patients is not related to gender, but some of its factors are related to age. Lipid profile is needed in patients with type 1 diabetes.

Keywords: lipid profile, triglycerides, type 1 diabetes

INTRODUCTION:

Type 1 diabetes is the most common endocrine-metabolic disorder of childhood and the nature of this disease and its prevalence is such that it brings irreparable biological, psychological, social and economic consequences, in other words, the basic components of human individual and social health. endangers, in such a way that it accounts for a high share of deaths caused by the disease in different societies (1). Type 1 and type 2 diabetes are chronic diseases that affect nearly 425 million people worldwide and lead to poor health outcomes and high healthcare costs (2). This number is expected to increase due to the growing rate of obesity, which contributes to the increased incidence of type 2 diabetes and the projected increase in the prevalence of type 1 diabetes globally (3, 4). Despite the different causes of type 1 and type 2 diabetes, both are associated with a number of complications on the cardiovascular system, kidneys, eyes, and nerves (5). Chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of various organs, especially eyes, kidneys, nerves, heart and blood vessels (6). Dyslipidemia is defined as increased levels of plasma triglycerides and cholesterol esters, which are components of low-density lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) cholesterol. Increased hepatic lipogenesis and fat tissue fatty acid metabolism in response to increased blood glucose and insulin resistance causes dyslipidemia in type 1 and type 2 diabetes (7, 8). Quantitative and qualitative lipid abnormalities are often present in people with type 1 diabetes and are related to blood sugar control (9). In type 1 diabetes, hypertriglyceridemia is also present, but when blood sugar control is good, HDL cholesterol levels may be normal or even elevated. In both types of diabetes, nephropathy is associated with exacerbation of hypertriglyceridemia, decrease in HDL cholesterol level and increase in serum cholesterol. (10, 11). Based on cross-sectional studies, it seems that dyslipidemia is more common among young people with diabetes than the general population of children (12, 13). And its relationship with blood sugar control has been repeatedly recorded (12, 14, 15). Studies on diabetic patients showed that the highest lipid levels are high levels of triglyceride, VLDL, LDL and total cholesterol (16). While increasing evidence suggests an important role for lipid metabolism in diabetes complications, future mechanistic studies will provide further insight into The contribution of dyslipidemia in kidney, eye and nerve damage caused by diabetes is needed (17).

The relationship between diabetes mellitus and insulin was discovered in the late 1950s, and it was suggested that people with this disease have different concentrations of insulin in their blood compared to healthy people (18).

Diabetes is a chronic disease in which body cells are unable to metabolize glucose, so the concentration of glucose in the blood increases and the person suffers from hyperglycemia. Insulin is the main hormone of glucose metabolism and the most important anabolic hormone in the human body. (19)

general complications of diabetes mellitus

Hyperglycemia occurs when the human body is not able to produce insulin or the sensitivity of the cells that consume glucose to insulin has decreased. Stable hyperglycemia can cause atherosclerosis in large vessels, and by causing microangiopathy of small vessels, it can cause kidney and eye dysfunction. Retinopathy and nephropathy are observed in almost all patients with chronic diabetes (20). Another side effect of persistent hyperglycemia is a change in fat and protein metabolism. Due to the inability to import glucose, body cells are forced to metabolize fats and proteins to provide the energy they need, and the by-products of their metabolism accumulate in the body and can eventually lead to acidification of the environment or ketoacidosis (21).

In a study conducted in 2019 by analyzing epidemiological information published in 138 different countries, the global prevalence of diabetes was estimated at 9.3 (22). Experts have predicted that diabetes mellitus will be the seventh leading cause of death by 2030 (23).

Type 1 diabetes:

This type of diabetes is an autoimmune disorder in which the body's immune system perceives insulin-producing cells in the pancreas as foreign agents and begins to destroy them. Therefore, the body does not have insulin-producing cells and will not be able to produce insulin. The prevalence of type 1 diabetes is around 5-10%. Symptoms of this disease usually appear quickly and are usually diagnosed in childhood and adolescence. Type 1 diabetes is a high-intensity disease that is usually controlled by insulin injections, and ketoacidosis is more likely to occur in this type of diabetes compared to other types.

Type 2 diabetes:

In this type of diabetes, the body produces the required insulin but is unable to use it. Its prevalence is around 90-95% and it is mostly observed in adults. Weight gain and inactivity are the underlying factors of this type of disease. Obesity and inactivity are the main risk factors of this disease, and compared to type 1, type 2 diabetes is considered a milder disease (21).

Gestational diabetes:

This type of diabetes is related to hormonal changes during pregnancy and is seen in women who have no history of diabetes (21).

Pathophysiology of diabetes:

Type 2 diabetes is characterized by insensitivity to insulin as a result of insulin resistance, decreased insulin production and finally the failure of pancreatic beta cells. This results in reduced glucose transport to the liver, muscle cells, and fat cells. There is an increase in fat breakdown with hyperglycemia (24, 25. A decrease in insulin receptor signaling leads to inhibition of Akt and dephosphorylation (activation) of GSK-3β and leads to tau (25, 26).

Prospective cohort studies have shown that increasing physical activity, independent of other risk factors, has a protective effect against the development of type 2 diabetes (27-29). Diet and lifestyle strategies include weight loss, improving blood sugar control, and reducing the risk of cardiovascular complications, which account for 70-80% of deaths among people with diabetes (30).

Diagnosis of diabetes:

Bickley and Szilagyi (2012) stated that to diagnose diabetes . Finally, additional tests, such as laboratory tests, can increase or decrease the probability of diagnosis (31). Laboratory tests for diagnosing diabetes include FPG, random glucose level, glucose tolerance test or OGTT, and HbA1c. For FPG test, the patient must avoid eating caloric substances for at least 8 hours. In normal state, FPG is <100 mg/dl. If FPG is greater than or equal to 100 mg/dl and less than 126, the patient is in pre-diabetes and if FPG is greater than or equal to 126 mg/dl in two separate tests, the diagnosis of diabetes is certain. If the patient's random glucose level is greater than or equal to 200mg/dl and the patient shows the cardinal symptoms of diabetes (drinking, excessive drinking, and weight loss), the diagnosis of diabetes is definite. A random glucose measurement is performed at any time regardless of the time of the last meal. (20).

The main advantage of the HbA1c test over other tests is that it shows the blood glucose status of the last three months, so it is the most valuable test for diagnosing uncontrolled diabetes. If HbA1c is less than 7%, diabetes is considered controlled (20).

Treatment of diabetes:
Insulin and oral hypoglycemic agents Insulin therapy should aim to mimic nature, which is highly successful in both limiting postprandial hyperglycemia and preventing intermeal hypoglycemia (32, 33). This is also due to the reduction of energy losses through glycosuria (34, 35). Acute administration of sulfonylurea in patients with type 2 diabetes increases insulin secretion from the pancreas and may also increase insulin levels by reducing the hepatic clearance of the hormone (36. Biguanides, like metformin, are antihyperglycemic, not hypoglycemic (37). Impairment of glucose absorption from the intestine has also been proposed as a mechanism of action (38-40).

Lipid profile and dyslipidemia:
Dyslipidemias are among the most common chronic diseases identified and treated. They are classically characterized by abnormal serum levels of cholesterol, triglycerides, or both, including abnormal levels of related lipoprotein species. The most common clinical outcome associated with dyslipidemia is an increased risk of atherosclerotic cardiovascular disease (ASCVD) (41).
TGs are an energy source for muscle and fat tissue. Cholesterol and TG circulate separately in the hydrophobic core of spherical lipoprotein particles, which are protected from the aqueous plasma by surface phospholipids and apolipoproteins (42). Lipoprotein species such as chylomicron (CM), very low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), LDL, and HDL are distinguished by characteristics such as function, size, density, relative lipid content, and definition. Apolipoproteins provide the latter components of particle stability and can act as ligands for receptors and as cofactors for processing and transporter molecules (42, 43).
Dietary cholesterol is absorbed by enterocytes in the upper part of the small intestine through the transporter Niemann-Pick C1-like 1 (44). In the liver, cholesterol can be obtained from plasma via lipoprotein absorption or it can be synthesized de novo through a multistep process(45). Free liver c is esterified in the form of cholesterol ester (CE) for transport in lipoproteins (46).
Dietary fatty acids are absorbed by enterocyte fatty acid transfer proteins and synthesized into TG by a multistep process involving diacylglycerol O-Acyltransferase (47). Packaging of TG and CE into nascent lipoproteins in the intestine and liver requires microsomal triglyceride transfer protein (48). In the intestine, the intracellular SAR1B GTPase protein encoded by the SAR1B gene is also essential for the aggregation of CM particles (49).
CMs pass through the lymphatic duct of the intestine and enter the blood circulation through the thoracic duct (50).Anchored binds to glycosylphosphatidyl linositol 1 (51). LPL activity is increased by apo C-II and apo A-V and inhibited by apo C-III (C3) and angiopoietin-like proteins 3 and 4 (52) Chylomicron remnants lacking TG are cleared by LDL receptor type 1 protein. It becomes (53).
Additional cholesterol enrichment after CE from HDL is exchanged for TG from apo B-containing lipoproteins, a process mediated by cholesterol ester transfer protein (CETP) (54). Further reduction of TG and enrichment of CE by hepatic lipase (HL) causes the production of LDL, which is finally cleared by hepatic LDL receptors (LDLRs) with the help of LDLR adapter protein 1 (LDLRAP1) (55) LDLRs are continuously recycled. (56).
HDL mediates the reverse transport of cholesterol from peripheral cells to the liver. Apo A-I (A1) containing pre-beta defatted HDL acquires cholesterol (57). HDL particles are endocytosed by scavenger receptor B1 (SR-B1) on liver cells, with cholesterol content towards secretion in bile (58).
Atherosclerosis begins in childhood (59), and early medical interventions, especially among children with FH, are now recommended by many opinion leaders to reduce long-term ASCVD risk (60). A universal screening program for FH at birth showed that for every 1000 newborns screened, 8 patients (4 children and 4 parents) were newly identified, which was considered a cost-effective approach (61). In contrast, a targeted approach to screen only those with a family history of lipid disorders or premature ASCVD failed to identify up to 60% of children at risk (89–91), although some have argued that targeting only children with a positive family . History is a maximum cost-effective approach. At the very least, a family history of a severe lipid phenotype or premature ASCVD should prompt consideration of cascade screening in children (62).

Adult screening:
Screening recommendations in adults similarly suffer from a lack of consensus. Some guidelines argue against universal screening in people without risk factors until at least age 40 (63,64)
Because it may be impossible to determine LDL-C in a statin-treated patient with persistently elevated TG, non-HDL-C, and/or apo B, alternative tests are for treatment thresholds and for monitoring treatment effects (65).
HDL is susceptible to chemical changes that alter its effectiveness in ASCVD prevention (66).
Lifestyle interventions such as improved diet and especially exercise appear to have clear benefits on HDL function, although as noted, this cannot be assessed by any current clinical method (67).
management of a patient with isolated low HDL-C consists of cautious lifestyle advice and drug therapy that focuses on optimal management of atherogenic apo-B-containing lipoproteins and uses statins as a first step (68)
Although some studies have shown that magnesium deficiency is associated with higher levels of LDL cholesterol, triglycerides, and lower levels of HDL

cholesterol, there was no significant difference in lipid profile parameters in this study. did not exist (69).

The results of the study confirmed the constant relationship between the increase in lipids and female sex, age, duration of diabetes, HbA1c and BMI. LDL and non-HDL cholesterol levels were lower in the pump therapy group compared to the injection therapy group (70). These findings emphasize the screening of lipid profiles in children and adolescents with type 1 diabetes (71).

The results of the study showed that the frequency of lumbar hypertriglyceridemia phenotype is related to women, atherogenic lipid profile and overweight, which indicates the importance of monitoring the nutrition of this population with the aim of reducing cardiovascular diseases in the future (72).

METHOD:

This research was a cross-sectional (descriptive-analytical) study that investigated the lipid profile of type 1 diabetic patients, 0-18 years old, referring to Ali Asghar Clinic in Zahedan.

Type 1 diabetes patients, 0-18 years old, who refer to the clinic, their lipid profile was checked. Patients with a history of hypothyroid disease, cholestasis, familial hypercholesterolemia, nephrotic syndrome, CRF, or receiving isoniazid, BB, estrogen, and clozapine drugs were excluded from the study. After collecting the data, the raw data was entered into the statistical software SPSS version 24. In the first step, the quality of the data was checked using graphical methods and the calculation of descriptive indices.

Frequency distribution tables and common statistical charts (bar or circle) were used to describe qualitative data. Also, to describe quantitative data, common central indices (mean and median) and dispersion indices (standard deviation and interquartile range) along with minimum and maximum were used. To estimate the frequency of lipid profile in type 1 diabetic children, point estimation and 95% interval were used. Also, these estimates were reported in different subgroups of society (gender and age). Chi-square test or Fisher's exact test was used to compare the ratio between groups (checking the assumption of independence). In all analyses, $P < 0.05$ was considered as the significance level.

Ethical considerations:

This study was approved by the ethics committee of Zahedan University of Medical Sciences with ID IR.ZAUMS.REC.1402.390.

FINDINGS OF THE STUDY:

The average age of the examined children was 10.46 ± 4.3 years with a range of 1 to 18 years. In terms of age distribution, 27 of the children (51.9%) were under ten years old and 25 of them (48.1%) were over 10 years old. In terms of gender distribution, 29 of the children (55.8%) were boys and 23 of them (44.2%) were girls.

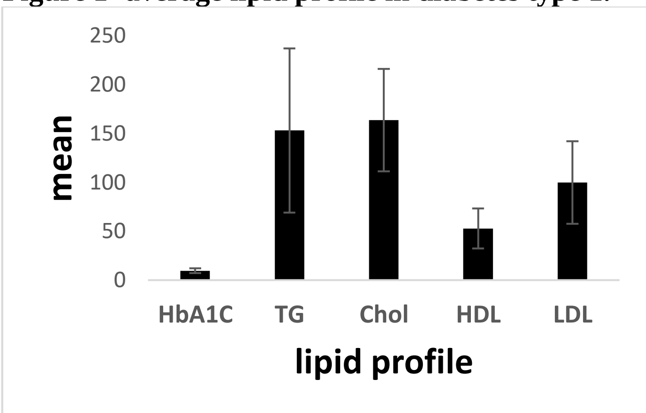
Table 1 shows the mean and standard deviation of the lipid profile of type 1 diabetic children referred to Ali Asghar Zahedan Clinic. This study showed that the average HbA1C, triglyceride, cholesterol, HDL and LDL in the examined children were 9.58 ± 2.5, 153.13 ± 84, 163.77 ± 52.5, and 78.20 ± 5, respectively. 52 and 42.3 ± 100 mg/dL.

Table-1 Mean and standard deviation of lipid profiles of type 1 diabetic children referred to Ali Asghar Zahedan Clinic.

Max	Min	SD	Mean	Lipid profile
18.9	4.5	2.5	9.58	HbA1C
416	36	84	153.13	TG
325	22	52.5	163.77	Chol
110	11	20.5	52.78	HDL
244	31	42.3	100	LDL

According to chart 1-, the highest average and the highest dispersion are related to the triglyceride variable

Figure 1- average lipid profile in diabetes type 1.



The second objective: to determine and compare the frequency of lipid profiles in type 1 diabetic children referred to Ali Asghar Clinic according to gender.

Table 2 shows the mean and standard deviation of the lipid profiles of type 1 diabetic children referred to Ali Asghar Zahedan Clinic by gender. The independent T-test showed that the average HbA1C and lipid profile do not differ according to gender, and none of these variables has a significant difference in boys and girls ($P<0.05$) (Table 2)

Table -2 Mean and standard deviation of lipid profiles of type 1 diabetic children referred to Ali Asghar Clinic.

P	SD	Mean	number	sex	
0.44	2.7	9.6	29	Male	HbA1C
	2.2	10.1	23	Female	
0.65	76.9	157.8	29	Male	TG
	93.7	147.2	23	Female	
	48.3	166.7	29	Male	Chol
0.65	58.2	160	23	Female	
0.99	24.5	52.7	29	Male	HDL
	14.7	52.7	23	Female	
0.87	47.1	99.2	29	Male	LDL
	36.3	101.2	23	Female	

The third objective: to determine and compare the frequency of lipid profiles in type 1 diabetic children referred to Ali Asghar Clinic according to age.
Table 3 shows the mean and standard deviation of the lipid profile of type 1 diabetic children referred to Ali Asghar Zahedan Clinic by age. The independent T test showed that there is no significant difference in HbA1C (P=0.069), cholesterol (P=0.07) and HDL (P=0.35) according to age, but the variables of triglyceride (P=0.033) and LDL (P=0.01) It varies according to age, so that the mean of triglyceride and LDL in children over ten years old is significantly higher than that of children under ten years old (Table 3).

Table -3 Mean and standard deviation of lipid profiles of type 1 diabetic children referred to Ali Asghar Zahedan clinic according to age.

P	SD	mean	number	Age	
0.069	2.4	9.2	27	Up to 10 yr	HbA1C
	2.5	10.5	25	Above 10 yr	
0.033	66.6	129.4	27	Up to 10 yr	TG
	94.3	178.7	25	Above 10 yr	
0.07	30.7	151.1	27	Up to 10 yr	Chol
	66.7	177.4	25	Above 10 yr	
0.35	19.8	55.3	27	Up to 10 yr	HDL
	21.5	50	25	Above 10 yr	
0.01	32.9	85.5	27	Up to 10 yr	LDL
	46.2	115.7	25	Above 10 yr	

This study showed that the average HbA1C, triglyceride, cholesterol, HDL and LDL in the examined children were 9.58 ± 2.5, 153.13 ± 84, 163.77 ± 52.5, and 78.20 ± 5, respectively. 52 and 42.3 ± 100 mg/dL.

DISCUSSION:

The study of Bhambhani et al. (2015) was conducted with the aim of investigating the lipid profile in diabetic patients in India, , The average TG in men was 125 and in women 139, the average HDL in men was 48 and in women 52, and the average LDL in men was 125 and in women was 126. 73) which was almost consistent with our study. (73) which was in a higher range compared to our study.
In the study of Meenu et al. (2013), which was conducted on 150 non-obese type 2 diabetes patients who had no history of high blood pressure in India, the mean and standard deviation of HbA1C, total cholesterol, TG and LDL were respectively 7.50 ± 1.44, 153.91 ± It was 34.08, 59.59 ± 152.81, and 32.05 ± 71.40, which was consistent with the present study. Also, the study of Kalsi et al. The average HDL was 35 ± 7 and the average was 164 ± 22. This study was also consistent with our study (74).
The study of Hashim (2015) was designed to determine the relationship between lipid profile levels in type 2 diabetes and high blood pressure in Iraq The results were that the mean and standard deviation of total cholesterol in women and men with type 2 diabetes were 163.33±23.69 and 204.71±28.99, respectively, and the average of TG in women and men. Diabetic was 39.97±123.19 and 45.77±123.21, and the average HDL was 7.592±47.333 and 5.898±47.000 in men and women, respectively (75). In general, it can be concluded from the above studies that the average lipid profile in diabetics is higher than in the non-patient population, so having a timely screening program for diabetic patients can be effective for timely identification of dyslipidemia.
In the present study, the independent T-test showed that the average HbA1C and lipid profile did not differ according to gender, and none of these variables had significant differences between boys and girls.
Kim et al.'s study (2014) was conducted with the aim of investigating serum lipid profile and blood sugar control in adolescents and young adults with type 1 diabetes (T1DM).The results showed that although dyslipidemia was more common in women than men, this finding was not statistically significant (50.0% [18/9 patients] vs. 18.2% [11/2 patients]; P=0.18) (76) which was consistent with the result of the present study.
Kosteria et al.'s (2019) study, which was conducted with the aim of investigating the lipid profile in children and adults with type 1 diabetes, showed that the level of LDL and non-HDL cholesterol was higher in girls than in boys (70).
In the study by Schwab et al. (2006), which was conducted with the aim of investigating the spectrum and prevalence of atherogenic risk factors in 27,358 children, teenagers and young adults with type 2 diabetes in Germany, high blood pressure, smoking and HDL cholesterol were observed more in men and an increase BMI, total cholesterol and LDL cholesterol were observed more in women (13). The study of Krantz et al. (2003) aimed to investigate the early onset of subclinical atherosclerosis in young people with type 1 diabetes in the United States on 142 patients with type 1 diabetes with an average age and 87 control subjects also showed that the level of lipids in girls was significantly higher than boys (77).
Marcovecchio et al.'s (2009) study, which aimed to investigate the abnormal lipid profile in adult patients with type 1 diabetes, was conducted on 890 type 1 diabetic patients in England. It showed that total cholesterol, LDL cholesterol, HDL cholesterol, and non-HDL cholesterol in women. It was more than men (P < 0.001) (78). On the contrary, the study of Abdul Majid (2019) and colleagues, which was conducted on 105 type 2 diabetes patients, showed that the total

cholesterol level is significantly related to gender and in There were more men (73) and this study was not consistent with the present study. In general, from the large difference in the results of the studies conducted on the relationship between gender and lipid profile in type 1 diabetic patients, it can be concluded that there is a need for much more studies in this field. There is a context.

The independent T-test showed that the mean of HbA1C (P=0.069), cholesterol (P=0.07) and HDL (P=0.35) did not differ significantly according to age, but the variables of triglyceride (P=0.033) and LDL (P=0.01) It varies according to age, so that the mean of triglyceride and LDL in children over ten years old is significantly higher than that of children over ten years old.

The study of Marcovecchio et al. (2009) showed that the amount of lipid profile increases with age (78), which was almost in line with our study. Therefore, as children age, it is better to perform lipid profile screening with less intervals.

Abdul Majid (2019) and colleagues mentioned in their study that HDL levels were significantly related to age, but other lipid profile components were not significantly related to age (73).

The study by Ladeia et al. was conducted in Brazil in 2019Ninety-four people (53.2% male), 15.4±4.7 years (21.9-3.6 years), with a disease duration of 5.0±3.6 years (17-0.3 years), were examined in terms of heart rate, blood pressure, height and weight. . Laboratory data include total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides (TGs), blood glucose, glycosylated hemoglobin (HbA1c), creatinine, thyroid-stimulating hormone, antibodies. Antithyroid, and -hourly microalbuminuria were correlated by Spearman's rank correlation test (79)

Final conclusion:

Finally, it can be stated that the level of lipid profile in type 1 diabetic patients is not related to gender, but some of its factors are related to age. Patients with type 1 diabetes are required.

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