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Research Article

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Cardiovascular Risk Factors among Libyan Children with Type 1 Diabetes Mellitus Attending Tripoli Children Teaching Hospital (2021)

Intisar Abulgassem[@1,2], Hanifa Alrabti[1,3], Faten Ben Rajab[1,2], Afaq Yousef[1,2], Jamila Diyab[1,3] and Ali Marzouq[1,4]

[1]Department of Pediatrics, Faculty of Medicine, University of Tripoli, Libya
[2]Endocrine Unit; [3]Cardiology Unit; [4]General Pediatric Ward, Tripoli Children Teaching Hospital, Libya

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ABSTRACT

Diabetes mellitus is associated with complications, and carries a significant premature mortality risk. Cardiovascular disease risk factors are more common in children with T1DM than in the general pediatric population. Risk factors are dyslipidemia, obesity and hypertension contribute to CVD risk in patients with T1DM.

To determine cardiovascular disease risk factors among children and adolescent aged less than 20 years with diabetes and estimate the effect of type I diabetes mellitus on cardiovascular system.

A cross-sectional study carried out on children with type 1 diabetes mellitus attending endocrine clinic in Tripoli Children Teaching Hospital from 1st of June to 31st of August 2021. The data was encoded and analyzed by SPSS version 22.

This study was included 100 children. The most frequent age was between 11 to 15 years accounted for 68% while 23% were between 16 to 20 years and 9% were between 5 to 10 years. 58% of patients were females. The diabetes duration was between 5 to 9 years accounted 51%. Nearly half of patients had uncontrolled diabetes mellitus (HbA1C. Mean HbA1C was 8.825 ± 2.046 SD. 45% of patients had received multiple daily insulin injections, 13% on flexible insulin regimen while 42% on insulin pump. Statistically significant results were reported between control of diabetes and method of therapy (*P*-value = 0.005). Majority of patients had normal body mass index while 21% were overweight and obese and 7% were underweight. 70% of patients were normotensive while 30% of them had hypertension. Only 4% of patients had hypothyroidism. 3% had high LDL (*P*-value = 0.003), 67% had high HDL, 8% had high TG and 5% had high cholesterol level (*P*-value = 0.000). Only one patient had retinopathy while 10% had mild nephropathy and 9% had moderate nephropathy. One patient had 1st degree heart block, one patient had flat T-wave and one patient had left ventricular hypertrophy on ECG.17% of patients had abnormal echocardiogram; 65.7% of them had uncontrolled diabetes. All patients had normal ejection fraction.

Conclusion: Type 1 DM among children and adolescents had several cardiovascular risks such as high LDL, TG and cholesterol level, hypertension and cardiovascular abnormalities; all these factors related to uncontrolled diabetes to some extent.

Keywords- *Cardiovascular; Children and Adolescent; Type 1Diabetes; Tripoli Children Hospital, Libya.*

INTRODUCTION

Type 1 diabetes mellitus (T1) creates substantial health burden, particularly due to its microvascular complications. Clinical awareness of diabetes-related microvascular complications in childhood and puberty is rare. Yet only a few years after onset of the disease, also some functional and structural abnormalities may already occur. As such, periodic screening for diabetic microvascular disease, namely retinopathy and nephropathy, assume centrality in pediatric diabetic care. Early functional and structural problems may be observed as soon as 2–5 years following diagnosis.[1]

Background retinopathy, which is not life-threatening and may or may not lead to more severe retinopathy, appears in almost all people with type 1 diabetes by the time the illness is 15 to 20 years old. While Preproliferative retinopathy is a strong indicator of the development of more severe retinopathy. A high risk of visual impairment from macular edema can be severe. Sensitive techniques (stereoscopic fundus photography or fluorescein angiography) are necessary to detect the earliest changes. Type 1 diabetes mellitus (T1DM) is the most common chronic disease in childhood, with good metabolic control during childhood and adolescence is critical for the future health and life quality of these patients.[2] Cardiovascular disease CVD risk factors are more common in children with T1DM than in the general pediatric population, and becoming major health issues among individuals with type 1 diabetes (T1DM) Various studies had shown that found girls appear to have a higher risk factor burden as a higher prevalence of high HbA1c, BMI, TC, LDL-C, and

@ Author to whom correspondence should be addressed: *Dr. Intisar Abulgassem*, Tel: *+218 915073724; E-mail:* intesar7373@gmail.com

BP, whereas boys were more likely to have low HDL-C.[3,4]

Globally, the incidence of cardiovascular disease (CVD) in persons with type 1 diabetes (T1DM) is substantially higher than in individuals without diabetes and is the leading cause of their morbidity and mortality traditional CVD risk factors, including dyslipidemia, overweight/ obesity, hypertension, and smoking, as contributors to CVD risk in patients with T1DM.[5] The risk of death from CVD in persons with T1DM with on-target glycemic control was more than twice the risk in the general population, and 10 times greater in subjects with poor glycemic control.[6]

Diabetes mellitus is associated with a premature CV mortality. Moreover, in patients with T1D, CV outcomes and mortality inversely correlate with age at diabetes onset; thus, suggesting that the earlier the onset, the greater risk.[7]

An albumin excretion rate (AER) of 20–200 mcg/min in two of three nighttime samples (obtained over a 6-month period) is known as microalbuminuria.

Diabetic retinopathy has a well-established natural history, thereafter, the aim should be to detect the appearance of high-risk retinopathy, and diabetic retinopathy may be classified into several stages.[8-10] Diabetes mellitus carries a high risk of premature death and is linked to severe morbidity from a number of comorbidities that tend to get worse over time. Diabetic nephropathy is a serious manifestation of diabetic angiopathy. It develops in about 35% of patients with type 1 diabetes. The incidence of nephropathy has decreased; most likely as a result of improved glycemic control.[11] Nephropathy affects a significant portion of people with type 1 diabetes mellitus, increasing their risk of dying young from cardiovascular disease and end-stage renal failure.[12]

Aims of the study:

1. To determine cardiovascular disease risk factors among children and adolescent aged less than 18 years with diabetes.

2. To Estimate the effect of type I diabetes mellitus on (cardiovascular system, heart, and blood pressure) in pediatric age group.

MATERIALS AND METHODS

A cross sectional study will be carried out on children suffer from type 1 diabetes mellitus attending outpatient clinic in Tripoli Children Hospital from 1st of June to 31st of August 2021.

***Study population and sampling*:**

A total of 100 study subjects will be included in the study through random sampling that attends the clinic during the study period. Every patient who met the inclusion criteria (patients of both sex, and use insulin injection for treatment, age 10years, and/ or diagnosed as type 1 diabetes mellitus 5years duration).

***Measure tool*:**

The data will be collected using questionnaire, which included the following information divided in to sections:

Section 1: Socio-demographic data were included; age, sex, duration of T1DM, insulin delivery method (insulin pump/injection as MDI or flexible regimen), and total daily insulin dose (U/kg/d).

Section 2: Clinical assessment and examination.

A. Anthropometric measurements which include: height will be measured in meter, weight in kilogram, and body mass index (BMI) calculation.

B. Arterial blood pressure for children and adults will be measured after sitting in silence for 5min in the left arm with appropriate cuff size. Hypertension defined as average systolic blood pressure SBP or diastolic blood pressure DBP that was greater than or equal to the 95th percentile for sex, age, and height on at least three separate occasions.

Section 3: Laboratory analysis as Glycosylated hemoglobin (HbA1c) and fasting lipid profiles will be measured and cutoff values of HbA1c 6.5-7.5 %.

Normal values for low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), and triglycerides (TG) defined as < 130 mg/dl, > 40mg/dl, and <150mg/dl, respectively. Normal values for total cholesterol defined as < 200mg/dl. If at least one lipid value was abnormal, dyslipidemia was considered to be present.[12]

Section 4: Evaluation of microvascular diabetes complication; all diabetic patients will be screen for the presence of retinopathy by ophthalmologist. Diabetic retinopathy will be identifying from stereoscopic fundus examination, for diabetic kidney damage will do albumin: creatinine ratio.

Section 5: Echocardiography and ECG in all patients involved in the study to evaluate cardiac function.

Data management and analysis:

The collected data will be sorted, coded then entered and analyzed using the SPSS statistical software. Descriptive statistics will be used to summarize the outcome variables. Appropriate inferential statistics will be done with *P*-value was set at $P < 0.05$ as statistically significant.

RESULTS

This study included 100 children suffer from type 1 diabetes mellitus attending outpatient clinic in Tripoli Children Hospital from 1st of June to 31st of August 2021.

***Age of children distribution*:**

Regarding the children age, the most frequent age was between 11 to 15 years accounted for 68.0% while 23.0% were between 16 to 20 years and 9.0% were between 5 to 10 years (Figure 1).

The mean age was 13.84 ± 2.359 SD with the minimum age was 7 years while the maximum age was 18 years.

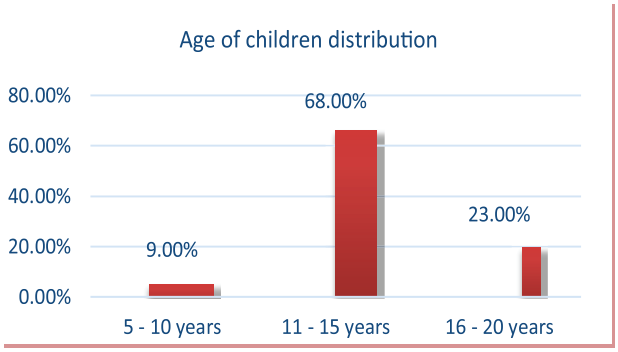

Figure 1: Age of children distribution, TCTH, Tripoli, Libya, 2021.

***Gender of children distribution*:**

Regarding the gender of children, 58.0% of patients were females while 42.0% of them were males (Figure 2).

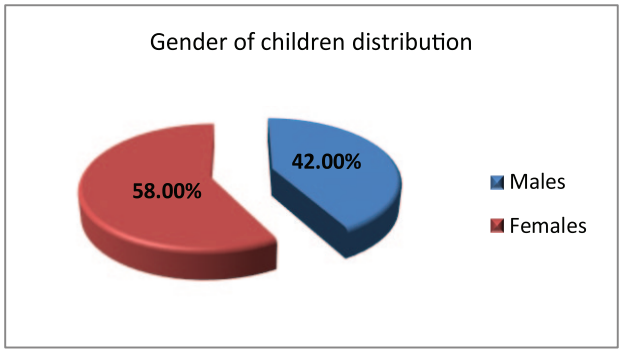

Figure 2: Gender of children distribution, TCTH, Tripoli, Libya, 2021.

***Duration of diabetes mellitus distribution*:**

Regarding the duration of diabetes mellitus, the most frequent duration was between 5 to 9 years accounted 51.0% (Figure 3). The mean duration was 6.13 ± 3.007 SD with the minimum duration was one year while the maximum duration was 13 years.

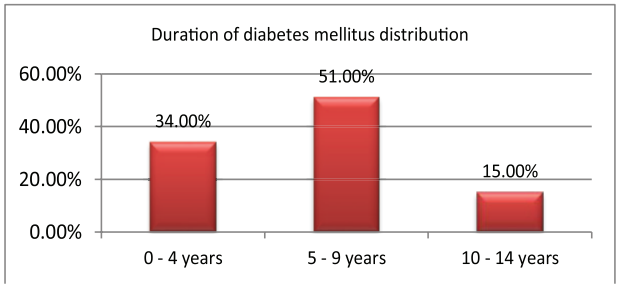

Figure 3: Duration of diabetes mellitus distribution, TCTH, Tripoli, Libya, 2021.

***Control of diabetes mellitus distribution*:**

Regarding the control of diabetes mellitus, nearly half of patients had uncontrolled diabetes mellitus accounted for 49.0% (Figure 4).

And the mean HbA1C was 8.825 ± 2.046 SD with the minimum level was 5.5% while the maximum level was 14.9%.

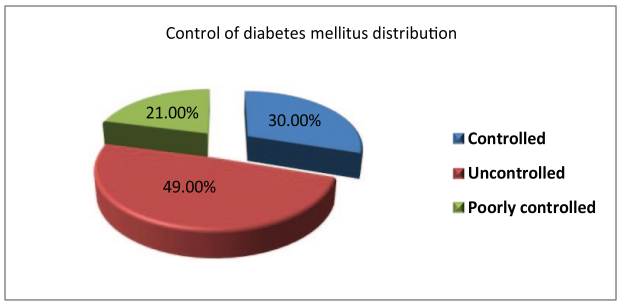

Figure 4: Control of diabetes mellitus distribution, TCTH, Tripoli, Libya, 2021.

***Method of diabetes mellitus treatment distribution*:**

Regarding the method of diabetes mellitus treatment, 45.0% of patients on MDI injections while 42.0% on insulin pump therapy and 13.0% had flexible insulin therapy (Figure 5).

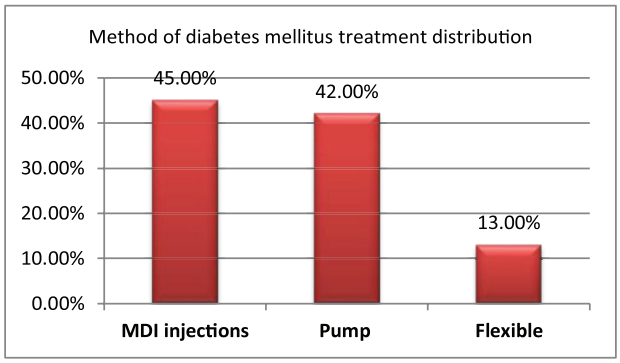

Figure 5: Method of diabetes mellitus treatment distribution, TCTH, Tripoli, Libya, 2021.

***Weight, height and body mass index measurements distribution*:**

Regarding the weight, height and body mass index measurements, the majority of patients had normal body mass index accounted 72.0% while 21.0% had overweight and obese and 7.0% had underweight (Figure 6).

And the mean weight was 51.08 ± 12.381 SD, mean height was 154.16 ± 10.398 SD and the mean body mass index was 21.38 ± 4.032 SD.

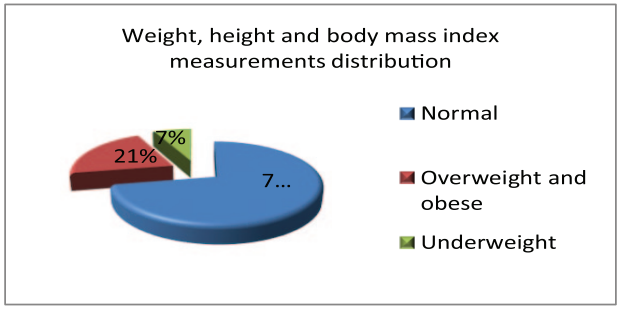

Figure 6: Weight, height and body mass index measurements distribution, TCTH, Tripoli, Libya, 2021.

***Associated co-morbidity distribution*:**

Regarding the associated Co-morbidity, 70.0% (70) of patients had normotensive while 30.0% of study participant had hypertension. The mean systolic blood pressure was 108.60 ± 10.574 SD with the minimum measurement was 80 while the maximum measurement was 135. And the mean diastolic blood pressure was 70.11 ± 9.620 SD with the minimum measurement was 50 while the maximum measurement was 100.

And just 4.0% (4) of patients had hypothyroidism.

***Fasting lipid profile distribution*:**

Regarding the fasting lipid profile, 3.0% had high LDL, 67.0% had high HDL, 8.0% had high TG and 5.0% had high cholesterol level (Table 1).

Table 1: Lipid profile distribution, TCTH, Tripoli, Libya, 2021.

Variables (n = 100)	Normal	High
LDL	97.0%	3.0%
HDL	33.0%	67.0%
TG	**92.0%**	8.0%
Cholesterol	95.0%	5.0%

***Retinopathy and nephropathy distribution*:**

Regarding the retinopathy and nephropathy, only one patient (1.0%) had retinopathy while 10.0% had mild nephropathy and 9.0% had moderate nephropathy (Table 2).

Table 2: Retinopathy and nephropathy distribution, TCTH, Tripoli, Libya, 2021.

Variables (n = 100)		%/F
Retinopathy		
	Yes	1.0%
	No	99.0%
Nephropathy		
	Normal	81.0%
	Mild	10.0%
	Moderate	9.0%

***Cardiovascular distribution*:**

Regarding the echocardiogram findings, 17.0% of participant had abnormal echocardiogram, all patients had normal ejection fraction function, and only one patient had physiological pericardial effusion but no dyskinesia or CHD or myocardial hypertrophy (Table 3).

And regarding the electrocardiogram picture, one patient (1.0%) had 1st degree heart block, one patient (1.0%) had flat T-wave and one patient (1.0%) had left ventricular hypertrophy (Table 3).

Table 3: Cardiovascular distribution, TCTH, Tripoli, Libya, 2021.

Variables (n = 100)		%/F
Echocardiogram		
	Normal	83.0%
	Abnormal	17.0%
Electrocardiogram		
	Normal	98.0%
	1st degree heart block	1.0%
	Flat T-wave	1.0%
Left ventricular hypertrophy		
	Yes	1.0%
	No	99.0%

***Relationship between control of diabetes mellitus and other variables distribution*:**

Statistical significant results reported between control of diabetes mellitus and method of therapy (*P*-value = 0.005), LDL (*P*-value = 0.003) and cholesterol (*P*-value = 0.000) but statistical insignificant results in other variables listed (Table 4).

Table 4: Relationship between control of diabetes mellitus and other variables distribution, TCTH, Tripoli, Libya, 2021.

Relationship of diabetes mellitus control with other variables	*P-value*
Age	0.345
Gender	0.491
Duration	0.287
Method of therapy	0.005
Hypertension	0.213
Hypothyroidism	0.967
LDL	0.003
HDL	0.652
TG	0.932
Cholesterol	0.000
LVH	0.308
Retinopathy	0.308
Nephropathy	0.584

DISCUSSION

Diabetes mellitus is associated with long term complications, and carries a significant premature mortality risk. The cardiovascular disease risk factors including dyslipidemia, obesity, and hypertension as contributors to CVD risk in patients with T1DM.[3,4] In this study 100 participant of type 1 diabetic children and adolescent with female predominance these results is similar to those in Stephanie Jones study.[14]

Regarding the age of participant the majority of cases ranged from 11years to 18 years with mean age 13.84 ±2.3 SD compared with study conducted by K Otfried Schwab *et al*.,[13] age at diabetic onset ranged from 8 to 9 years. In our participant 66% had diabetes more than 5 years mean duration 6.13 ± 3.007 SD compared with K Otfried Schwab *et al*., study[13] diabetes duration from 4.1-6.6 years with mean HbA1c was 8.5 ± 2%; Ingrida Stankute *et al*.,[15] in comparison with our study mean HbA1c is 8.825 ± 2.046 SD, the hypertension were seen in 30%of our participant in Stephanie Jones *et al*.,[14] study 20.5% were hypertensive (elevated diastolic blood pressure) there is significant associations between diabetes duration and annual increases BP (0.1 SD score), study subjects' hypertension were diagnosed in 29.8% of participants. Hypertension was more prevalent in overweight and obese compared to normal-weight patients (40.6 and 65.6 vs. 25.6%, respectively, *P* < 0 001) in Ingrida Stankute *et al*., study.[15] The treatment method is different shows that the pump therapy is the best treatment modality in our study participant in term of glycemic control *P*-value<0.001. The obesity and over weight is seen in 21% of participant nearly similar to Ingrida Stankute study that shows 19.5% were overweight and 3.6% obese and our results remarkably lower than Stephanie Jones et al.,[14] 33.8% of children were overweight or obese, with significant associations between diabetes duration and annual increases of body mass index (0.6 kg/m2), the fasting lipid profile screening in study participant shows low density lipoprotein cholesterol, triglyceride, total cholesterol were disturbed and abnormal in 3%, 8%, 5% respectively. And relation between LDL and diabetic control the *P*-value = 0.003 which is statistically significant, and relation between total cholesterol and diabetic control the *P*-value =0.000 lower than the results of Stephanie Jones study,[14] total cholesterol, low-density lipoprotein-cholesterol and high-density lipoprotein-cholesterol were abnormal in 63.5%, 34.2% and 22.0%, respectively. With significant associations between diabetes duration and dyslipidemia (0.02–0.06 mmol/L) were noted.

High density lipoprotein which is elevated in 67% of study participant is good protective factor from cardiovascular disease and atherosclerosis. In our study the relation between nephropathy and hypertension was non-significant with *P*- value = 0.094 compared with Ingrida Stankute etal the frequency of microvascular complications was higher among patients with dyslipidemia (27.2 vs. 18.8%, *P* = 0 005) and among those with hypertension (25.9 vs. 23.2%, *P* < 0 001).

Compare our study with study conducted by Ingrida Stankute *et al*.,[15] results of study subjects' dyslipidemia were diagnosed in 62.6% of participants, respectively. HbA1c concentration was directly related to levels of total cholesterol (r = 0 274, *P* < 0 001), LDL (r = 0 271, *P*< 0 001), and triglycerides (r = 0 407, *P* < 0 001) and inversely associated with levels of HDL (r = 0 117, *P* = 0 001). Prevalence of dyslipidemia increased with duration of diabetes (*P* < 0 05). In K Otfried_Schwab *et al*.,[13] study 65% had no or 1 cvRF. HbA1c >/=7.5% was the most frequently occurring cvRF followed by BP >or=90th percentile, dyslipidemia, and BMI >97th percentile. CvRF showed differences in disfavour of females except HDL-C <35 mg/dL (0.91 mmol/L).

On other hand compared with study done by Jonathan Schofield and his colleague[7] the cardiovascular mortality in T1DM suggested that risk only significantly increases after the development of nephropathy, which associated with a marked deterioration of the lipid profile and blood pressure (BP), while features such as the presence of nephropathy or retinopathy identify higher risk groups. The abnormal echocardiography were seen in 17% which means tricuspid regurgitation is pathological if RVP>25mmHg, aortic regurgitation and mitral regurgitation is

pathological if associated with high BP and/or LVH our study fails to reach statistically significant association echocardiogram findings and HbA1c level with *P* -value = 0.817 compare to previous study by Faten M Abd-El Aziz *et al*.,[16] which was significant relation between echocardiography and diastolic dysfunction in diabetic children.

CONCLUSION

This study had concluded that the type 1 diabetes mellitus among children had several cardiovascular risks such as abnormal lipid profile, hypertension and cardiovascular abnormalities; all these factors related to poor glycemic control as well as long duration of disease to some extent.

Insulin pump therapy is the best treatment modality in our participant.

Recommendation:

-longitudinal study for long period of time is needed to give more information about glycemic control and diabetes complication. Modifiable risk factors for cardiovascular complication as dyslipidemia, hypertension, and obesity control must be closely monitored; strict glycemic control and adequate diabetes management are essential approach to reduce related morbidity and mortality. Microvascular complication such as diabetic nephropathy and retinopathy should be a part of annual screening.

Ethical Approval:

The study was approved by the Tripoli Children's Hospital Committee for scientific research, and permission was also obtained from the research and consulting department

at the Faculty of Medicine, University of Tripoli for publications. Verbal informed consent was obtained from all participants during their follow-up at the clinic. Data confidentiality was maintained throughout the study and any resulting publication anonymously.

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