Review Article

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Dyslipidemia and Cardiovascular Risk in Pediatric and Adolescent Type 1 Diabetes Mellitus: A Systematic Review

Sayema Ainan[1*]

ABSTRACT

Background: Dyslipidemia, characterized by abnormal lipid profiles, is a significant Cardiovascular Risk Factor (CVRF) in the general population and its presence in children and adolescents with Type 1 Diabetes Mellitus (T1DM) is a major concern. The clinical profile of diabetes in children and adolescents under eighteen years of age often includes various complications and associated conditions, demanding comprehensive management. In regions like Bangladesh, T1DM presents unique challenges in terms of incidence and care. Multiple studies have highlighted a considerable prevalence of dyslipidemia in this young T1DM population, with rates varying across different geographical and ethnic cohorts. The primary abnormalities observed typically involve elevated levels of Total Cholesterol (TC) Triglycerides (TG) and Low-Density Lipoprotein Cholesterol (LDL-C), coupled with reduced high-density lipoprotein cholesterol (HDL-C). A strong and consistent association has been established between poor long-term glycemic control, particularly indicated by High Glycosylated Hemoglobin (HbA1c) levels and adverse lipid profiles. Diabetes duration is also often implicated, with longer duration correlating with worse dyslipidemia, thereby accelerating the progression of subclinical atherosclerosis detected early in T1DM youth. Other factors such as body habitus, which can be assessed via anthropometric measurements, and certain dietary intakes may also influence lipid status. The significance of these lipid abnormalities lies in their role in the development of premature atherogenesis and subsequent cardiovascular events. Consequently, there is an established need for rigorous screening, as recommended by major professional bodies and the implementation of therapeutic strategies. Recent findings, including randomized controlled trials, suggest that non-pharmacological interventions like regular exercise can potentially improve cardiovascular risk factors in these adolescents.

Methodology: This current study is a systematic review to the published articles and research studies carried out via PubMed and Google scholar. Strategy for article search was by using appropriate key words and title.

Conclusion: This systematic review synthesizes the current literature to emphasize the burden of dyslipidemia, its key determinants (Poor glycemic control, diabetes duration etc.) and the imperative for early risk mitigation in pediatric and adolescent T1DM. The overall implication is the need for rigorous screening and therapeutic strategies to prevent premature cardiovascular events.

KEY WORDS
Adolescents; Cardiovascular risk factors; Dyslipidemia; Glycemic control; Type 1 Diabetes Mellitus.

INTRODUCTION

Type 1 Diabetes Mellitus (T1DM) is an autoimmune disorder that results in the destruction of pancreatic beta cells, leading to absolute insulin deficiency.[1] The global incidence of T1DM is rising, with a particular increase noted even in Non-Insulin-Dependent forms (NIDDM, now T2DM) among adolescents, highlighting a shifting epidemiological landscape in pediatric diabetes.[2] In the context of developing nations like Bangladesh, T1DM is a growing public health concern, where its perspective and management pose distinct challenges.[1,3] The clinical profile of diabetes in children and adolescents under eighteen years of age encompasses a spectrum of metabolic and physiological changes that require specialized care and monitoring.[3]

One of the most critical long-term complications of T1DM is the accelerated development of Cardiovascular Disease (CVD) which is the leading cause of morbidity and mortality in adults with diabetes.[4,5] Dyslipidemia, defined as abnormal concentrations of lipoproteins in the blood, is a major,

1. Associate Profesor of Physiology
Brahmanbaria Medical College, Brahmanbaria.
*Correspondence : Dr. Sayema Ainan
Email: sayema.ainan@gmail.com
Cell : +88 01741761131

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modifiable Cardiovascular Risk Factor (CVRF) that significantly contributes to atherogenesis.[6,7] Studies indicate that dyslipidemia is a major risk factor in cardiovascular disease, particularly in diabetic patients.[6] The nature of dyslipidemia in T1DM typically involves alterations in all major lipid fractions, primarily an increase in atherogenic lipoproteins and a decrease in protective ones.[7] Furthermore, the long-term impact of hyperglycemia on the natural history of cardiovascular disease is well-documented.[4] Therefore, understanding the prevalence, determinants and management of dyslipidemia in the young T1DM population is paramount for prevention of premature CVD.[5,8] This systematic review aims to comprehensively analyze data from recent studies to characterize dyslipidemia in children and adolescents with T1DM, focusing on its relationship with glycemic control, duration of diabetes, and other relevant risk factors, as well as discussing therapeutic modalities.[9-12]

SEARCH STRATEGY

This systematic review was conducted based on a focused selection of thirty-three peer-reviewed articles, theses and expert panel reports concerning Type 1 Diabetes Mellitus, dyslipidemia and cardiovascular risk factors in children and adolescents.[1,13] Prevailing studies and abstracts were identified through PubMed and Google scholar (1990-2024). Key search topics was dyslipidemia and Cardiovascular Risk in Type 1 diabetes. The review synthesized information, data and findings from these primary sources to establish the prevalence, clinical correlations and management approaches for dyslipidemia in this type 1 diabetes. Data regarding clinical profiles, biochemical analyses (Lipid parameters, HbA1c) and intervention outcomes were also extracted. The collected data were organized into thematic sections to facilitate discussion.

DISCUSSION

The Epidemiological and Clinical Profile of Pediatric T1DM

The prevalence and clinical characteristics of T1DM are important for contextualizing associated comorbidities.[1] In Bangladesh, T1DM, while less common than Type 2 Diabetes Mellitus, is a significant endocrine disorder whose perspective warrants dedicated attention.[1] The clinical profile of diabetes mellitus in children and adolescents under eighteen years of age shows distinct features compared to adult-onset diabetes, requiring specialized management.[3] Moreover, the shifting landscape of pediatric diabetes includes an observed increased incidence of Non-Insulin-Dependent Diabetes Mellitus (NIDDM) or Type 2 Diabetes, among adolescents, further complicating the risk stratification for cardiovascular disease.[2]

Prevalence and Characteristics of Dyslipidemia

Dyslipidemia is highly prevalent among children and adolescents with T1DM, and its presence is a significant finding even in pediatric populations.[9,14] The lipid profile abnormalities in T1DM are central to the accelerated risk of cardiovascular disease.[15,7] The specific abnormalities generally include an increase in Total Cholesterol (TC) Low-Density Lipoprotein Cholesterol (LDL-C) and Triglycerides (TG) with a corresponding decrease in the cardioprotective High-Density Lipoprotein Cholesterol (HDL-C)[9,12,16] This pattern is consistent with the pro-atherogenic changes described in reviews of dyslipidemia in diabetes mellitus.[7] Studies indicate that dyslipidemia often comprises a spectrum of abnormalities, with elevated TC being a common finding.[17,14]

Surveys conducted across various countries and regions indicate substantial heterogeneity in the reported prevalence rates of dyslipidemia in this young cohort.[18-20,14] For instance, studies have reported varying prevalence rates:

- In Sudan's Khartoum state, the prevalence of dyslipidemia in children with T1DM was approximately 46%.[18]
- In Iran, a study reported a prevalence of dyslipidemia of 56.5% in children and adolescents with T1DM.[20]
- In Erbil governorate, Iraq, another study on children with T1DM reported a dyslipidemia prevalence of 65.2%.[19]
- A broader European study on a large cohort found that up to 34% of children, adolescents and young adults with T1DM had at least one atherogenic risk factor.[14]

Other regional studies, such as those in Iraq, Egypt and a general review of young T1DM patients, also confirm the significance of lipid abnormalities in this population.[9,21,17] The significance of lipid abnormalities in children with insulin-dependent diabetes mellitus is a long-recognized issue.[21] This high prevalence underscores the urgent need for regular monitoring and management, as emphasized by guidelines for children and adolescents with diabetes.[22] A significant portion of young adults with T1DM are reported to be unaware of or not treated for their dyslipidemia, indicating a gap in care.[23]

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Table I Profile of Dyslipidemia Abnormalities in Young Patients with Type 1 Diabetes Mellitus[9,15,12,7,16,17,14]

Type of Abnormality	Common Findings in T1DM Youth	Associated Risk/Significance
Total Cholesterol (TC)	Elevated (Hypercholesterolemia)	General marker of cardiovascular risk
LDL-C	Elevated (Primary atherogenic lipoprotein)	Directly contributes to atherosclerotic plaque
Triglycerides (TG)	Elevated (Common in poor control and insulin resistance)	Independent risk factor, part of diabetic dyslipidemia
HDL-C	Decreased (Reduced cardiac protection)	Loss of anti-atherogenic and reverse cholesterol transport effect

Determinants of Dyslipidemia: Glycemic Control and Disease Duration

The primary and most frequently investigated correlating factor for dyslipidemia in T1DM is the quality of glycemic control.[9,15,11] Poor glycemic control, which is best reflected by elevated levels of Glycosylated Hemoglobin (HbA1c), is strongly and positively correlated with adverse lipid profiles[9,15,24,25] Multiple studies in adolescents and young adults confirm that elevated HbA1c is a reliable predictor of abnormal lipid status.[11,16]

Elevated HbA1c is linked to high levels of TC and LDL-C and often inversely related to protective HDL-C.[11,24,25] The correlation between glycosylated HbA1c and plasma lipoproteins was documented as early as the 1980s in juvenile onset diabetes mellitus.[25] High HbA1c, signifying prolonged hyperglycemia, is recognized as a major risk factor for dyslipidemia and subsequent cardiovascular complications.[5,4] Studies on children with insulin-dependent diabetes mellitus confirm that poor glycemic control is associated with lipid abnormalities.[24] The severity of microvascular and neuropathic complications in diabetes is also linked to suboptimal glycaemic control, further underscoring the systemic nature of metabolic dysregulation.[26] Importantly, while HbA1c is the dominant factor, studies have noted that even children with good glycemic control may still exhibit dyslipidemia and lipid peroxidation, suggesting that residual risk factors and metabolic imbalances persist.[27]

Disease duration is another critical epidemiological risk factor for dyslipidemia.[9,15] Several studies have established that a longer duration of T1DM is associated with a greater degree of dyslipidemia, particularly elevated TC and LDL-C.[9,15,12] The natural history of cardiovascular disease in diabetes shows that hyperglycemia plays a key role and the cumulative exposure over time contributes to complications.[4] This progressive accumulation of lipid abnormalities is particularly alarming because it contributes to the early onset of subclinical atherosclerosis detected in young persons with T1DM.[8]

Other Contributing and Correlating Factors

Other factors beyond core metabolic control are also recognized to modulate the lipid profile in T1DM youth.[9] These factors include body composition and dietary habits.

- **Body Habitus and Anthropometry:** The relationship between body habitus and dyslipidemia is frequently explored in T1DM cohorts.[9,11] Dyslipidemia has been shown to relate to body habitus, especially in terms of Body Mass Index (BMI) and other anthropometric measurements.[9,28] The relationship between anthropometric and biochemical profiles in children and adolescents with T1DM suggests that measures of adiposity are relevant risk factors.[28] Evaluation of risk factors for atherosclerosis, including hypercholesterolemia, in children with T1DM also includes the assessment of physical measurements, reinforcing their role in overall risk evaluation.[13]
- **Dietary Factors:** Dietary intake is consistently investigated as a potentially modifiable factor contributing to dyslipidemia.[9] While diet is integral to diabetes management, one study suggested that general dietary fats may not be the primary contributor to hyperlipidemia in children and adolescents with T1DM, postulating that metabolic control exerts a more profound influence.[29] However, a comprehensive assessment of dietary intake, including both quality and quantity, remains a necessary component of epidemiological and management assessments.[9]

Pathophysiology and Cardiovascular Consequences

The abnormalities in lipoprotein concentrations in diabetes are the main driver of accelerated atherogenesis.[7] Diabetic dyslipidemia is typically characterized by an increase in atherogenic lipoproteins, such as a predominance of small, dense LDL particles, and decreased anti-atherogenic HDL-C.[7] This metabolic milieu, exacerbated by poor glycemic control and insulin resistance, accelerates the natural history of cardiovascular disease.[4] These lipid abnormalities are considered a major risk factor.[6]

The consequence of this chronic exposure to dyslipidemia and hyperglycemia is the early onset of subclinical atherosclerosis.[8] The lipid profile abnormalities correlate strongly to overall cardiac risk factors and cardiovascular function in adolescent diabetics from developing countries, highlighting its early diagnostic and prognostic importance.[11] The National Heart, Lung, and Blood Institute of Diabetes and Digestive and Kidney Diseases Working Group officially reported on the serious risk of cardiovascular complications in Type 1 Diabetes Mellitus, stressing the need for targeted prevention.[5]

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Table II Conceptual Link between Glycemic Control, Dyslipidemia and Atherogenesis in T1DM Based on findings showing the role of hyperglycemia, lipid abnormalities and progression to complications[7,4,5,8]

Component	Description	Consequence
Chronic Hyperglycemia	Metabolic dysfunction due to poor glycemic control (High HbA1c, high glucose levels)	Primary upstream driver of lipoprotein changes
Diabetic Dyslipidemia	Increased Small, Dense LDL-C/TC/TG, Decreased HDL-C	Pro-inflammatory and pro-thrombotic state, accelerated endothelial damage
Endothelial Dysfunction	Impaired vascular function due to metabolic stress and lipid deposition	Initiation of atherosclerotic plaque formation and vessel stiffness
Subclinical Atherosclerosis	Detectable early changes (e.g. Increased carotid intima-media thickness)	Increased risk of future clinical Cardiovascular Disease (CVD) events

Screening and Management of Dyslipidemia

Given the significant and premature cardiovascular risks, established guidelines from major professional bodies mandate regular screening and management.[30,22] The National Cholesterol Education Program (NCEP) Expert Panel's Adult Treatment Panel III (ATP III) provided comprehensive foundational guidelines for managing high blood cholesterol.[30] Building on this, the American Diabetes Association (ADA) developed specific recommendations for the management of dyslipidemia in children and adolescents with diabetes.[30]

However, data suggests that the implementation of these guidelines may be inconsistent. Studies have reported that awareness and subsequent treatment of dyslipidemia in young adults with T1DM is often inadequate.[23] Longitudinal lipid screening and the consistent use of lipid-lowering medications in pediatric T1DM require more focused attention.[31] Comparing lipid and lipoprotein profiles in youth with and without T1DM confirms the necessity of targeted, early and consistent screening in the diabetic group.[32]

Therapeutic strategies focus on optimizing glycemic control as the primary intervention, followed by lifestyle modifications and if necessary, pharmacological agents.[22]

- **Role of Exercise:** Non-pharmacological interventions are crucial. A randomized controlled trial investigated whether exercise could serve as a therapeutic tool for improving cardiovascular risk factors in adolescents with T1DM.[10] The study provided evidence that regular physical activity can lead to improvements in various cardiovascular risk factors, suggesting that exercise is a valuable, safe, and effective part of a management strategy.[10]
- **Pharmacological and Adjuvant Therapy:** When lifestyle measures are insufficient, pharmacological intervention is indicated according to guidelines.[22] Furthermore, studies have also explored adjuvant therapies. Research has been conducted on the use of antioxidant therapy in T1DM children, particularly those who demonstrate dyslipidemia despite having good glycemic control.[27]

CONCLUSION

Dyslipidemia is a highly prevalent and critical cardiovascular risk factor in children and adolescents with Type 1 Diabetes Mellitus (T1DM) contributing significantly to the early development of subclinical atherosclerosis.[18,14,8] The core drivers of adverse lipid profiles are poor glycemic control, as indicated by elevated HbA1c, and a longer duration of diabetes.[9,15,11,24] While dietary factors and body habitus are co-morbid factors, metabolic control remains the most powerful and modifiable predictor of lipid status.[9,29,28] Given the significant long-term morbidity and mortality associated with cardiovascular disease in this population, rigorous screening protocols and effective intervention strategies are essential.[22,5,23] Lifestyle modifications, particularly the inclusion of regular exercise, offer a viable and evidence-backed therapeutic tool for improving cardiovascular risk profiles.[10] Future efforts must focus on improving awareness, adherence to screening guidelines, and timely initiation of both non-pharmacological and pharmacological treatments to mitigate the progressive cardiovascular risk in young individuals with T1DM.[23,31]

DISCLOSURE

The author declared no competing interests.

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