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ORIGINAL RESEARCH

Risk of cardiovascular disease in adolescents with severe obesity

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Abstract
Adolescent obesity is a growing global health concern, with severe obesity significantly increasing the risk of early-onset cardiovascular disease (CVD). The association between obesity and CVD stems from multiple pathophysiological mechanisms, including insulin resistance, dyslipidemia, chronic inflammation, hypertension, and endothelial dysfunction. These factors contribute to accelerated atherosclerosis, left ventricular hypertrophy, and long-term cardiovascular complications. Early screening using clinical markers such as blood pressure, lipid profiles, and inflammatory biomarkers, along with imaging techniques like echocardiography and carotid intima-media thickness (CIMT) measurement, is essential in identifying at-risk individuals. Prevention and management strategies primarily focus on lifestyle modifications, including dietary improvements, increased physical activity, and behavioral therapy. Pharmacological interventions, such as metformin for insulin resistance and statins for dyslipidemia, may be warranted in select cases, while bariatric surgery is considered for adolescents with severe obesity and significant comorbidities. Despite these interventions, there remain significant research gaps, particularly in the long-term outcomes of obesity-related cardiovascular disease, the potential role of novel therapies such as GLP-1 receptor agonists, and the influence of genetic and epigenetic factors. Additionally, advancements in digital health tools, including wearable technology and AI-driven monitoring systems, hold promise for personalized risk assessment and management. A multidisciplinary approach integrating clinical care, community-based initiatives, and policy changes is crucial to addressing the obesity epidemic and reducing the future burden of cardiovascular disease in adolescents. Further research is needed to develop targeted interventions and optimize treatment strategies for this vulnerable population.
Keywords: Adolescent obesity, cardiovascular disease, insulin resistance, dyslipidemia, hypertension, atherosclerosis, left ventricular hypertrophy, prevention, management, screening.

Introduction
Severe obesity in adolescents is defined as having a Body Mass Index (BMI) ≥120% of the 95th percentile for age and sex, or a BMI ≥35 kg/m², according to the Centers for Disease Control and Prevention (CDC) guidelines [1]. It is a critical public health concern due to its long-term impact on metabolic and cardiovascular health. Unlike mild or moderate obesity,

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severe obesity in adolescents is associated with rapid disease progression, increasing the risk of premature cardiovascular disease (CVD) in adulthood [2].

Rising Global Prevalence of Adolescent Obesity

The prevalence of adolescent obesity has increased significantly over the past decades, with an estimated 124 million children and adolescents worldwide classified as obese [3]. Socioeconomic disparities, sedentary lifestyles, and the consumption of calorie-dense, nutrient-poor diets have exacerbated this crisis. Developing nations, traditionally burdened with undernutrition, now face a double burden of malnutrition where obesity coexists with micronutrient deficiencies [4].

Connection Between Obesity and Cardiovascular Risk Factors

Severe obesity in adolescents is strongly associated with cardiovascular risk factors, including hypertension, dyslipidemia, insulin resistance, and systemic inflammation [5]. Early vascular changes, such as arterial stiffness and endothelial dysfunction, can be detected in obese adolescents, demonstrating that atherosclerosis begins in childhood [6].

Importance of Early Intervention

Since obesity-related cardiovascular complications are cumulative and progressive, early identification and intervention are crucial. Lifestyle modifications, pharmacotherapy, and, in some cases, bariatric surgery have been proposed to mitigate long-term risks [7]. Without appropriate management, adolescents with severe obesity are at high risk of developing premature coronary artery disease (CAD), heart failure, and stroke in early adulthood [8]. This underscores the urgency of targeted preventive strategies in clinical, community, and policy settings to combat the obesity epidemic.

Pathophysiology of Severe Obesity and Cardiovascular Risk

The development of cardiovascular disease in adolescents with severe obesity is multifactorial, driven by metabolic, hormonal, and inflammatory alterations that lead to vascular dysfunction and cardiac remodeling [9].

Metabolic and Physiological Changes in Severe Obesity

Adolescents with severe obesity exhibit altered energy metabolism due to leptin resistance, insulin resistance, and chronic low-grade inflammation [10]. Excess adipose tissue leads to dysregulated lipid and glucose metabolism, triggering early onset atherosclerosis and cardiac dysfunction. Visceral fat accumulation is particularly concerning, as it contributes to increased free fatty acids (FFA), lipotoxicity, and ectopic fat deposition in organs such as the liver and heart [6].

Insulin Resistance and Its Role in CVD

Insulin resistance, a hallmark of obesity, leads to hyperinsulinemia and compensatory β-cell dysfunction, increasing the risk of type 2 diabetes mellitus (T2DM) and cardiovascular complications [4]. Chronically elevated insulin levels promote vascular smooth muscle proliferation and arterial stiffness, predisposing individuals to hypertension and endothelial dysfunction. In addition, insulin resistance impairs nitric oxide (NO) bioavailability, reducing vasodilation and accelerating atherogenesis [3].

Dyslipidemia and Atherosclerosis

Obese adolescents frequently develop dyslipidemia, characterized by elevated triglycerides, low high-density lipoprotein (HDL), and increased low-density lipoprotein (LDL) [5]. These

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lipid abnormalities contribute to atherosclerotic plaque formation, arterial wall thickening, and increased cardiovascular risk. Studies have shown that obese adolescents already exhibit early signs of carotid artery intima-media thickness (CIMT), a surrogate marker for atherosclerosis [6].

Hypertension and Endothelial Dysfunction

Hypertension in obese adolescents is driven by sympathetic nervous system overactivity, increased sodium retention, and activation of the renin-angiotensin-aldosterone system (RAAS) [8]. The resultant elevated blood pressure (BP) increases shear stress on arteries, promoting endothelial dysfunction and vascular remodeling. Endothelial dysfunction, an early marker of CVD, is characterized by reduced NO production, increased oxidative stress, and chronic inflammation [7].

Chronic Inflammation and Oxidative Stress

Obesity is associated with chronic low-grade inflammation, mediated by pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP) [9]. These inflammatory mediators contribute to vascular damage, insulin resistance, and myocardial dysfunction. Furthermore, oxidative stress exacerbates endothelial injury, increasing the likelihood of early-onset cardiovascular complications in obese adolescents [10].

In summary, the interplay of insulin resistance, dyslipidemia, hypertension, inflammation, and oxidative stress creates a pro-atherogenic and pro-hypertensive state in adolescents with severe obesity. These mechanisms accelerate cardiovascular disease progression, making early diagnosis and management critical in preventing long-term morbidity and mortality.

Cardiovascular Complications in Adolescents with Severe Obesity

Adolescents with severe obesity are at a significantly higher risk of developing cardiovascular complications, many of which were previously thought to be diseases of adulthood. The interplay of hypertension, dyslipidemia, insulin resistance, and chronic inflammation accelerates cardiovascular damage, leading to early-onset atherosclerosis, cardiac dysfunction, and structural heart disease [1].

Hypertension: Mechanisms and Long-Term Impact

Hypertension is one of the most common cardiovascular complications observed in obese adolescents. The renin-angiotensin-aldosterone system (RAAS) is overactivated, leading to increased sodium retention, fluid overload, and elevated blood pressure (BP) [2]. Additionally, sympathetic nervous system overactivity and chronic inflammation contribute to persistent vasoconstriction and arterial stiffness. If left untreated, childhood hypertension can progress to hypertensive heart disease, stroke, and chronic kidney disease in early adulthood [3].

Dyslipidemia: Role of High LDL and Low HDL

Obese adolescents commonly develop atherogenic dyslipidemia, characterized by:

- Elevated low-density lipoprotein (LDL-C), which promotes cholesterol deposition in arteries.
- Decreased high-density lipoprotein (HDL-C), reducing the clearance of cholesterol from circulation.
- Increased triglycerides, contributing to lipid oxidation and endothelial dysfunction [4].

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The combination of high LDL and low HDL levels promotes early atherosclerotic plaque formation, increasing the risk of coronary artery disease (CAD) and cerebrovascular complications later in life [5].

Insulin Resistance and Type 2 Diabetes: Impact on Heart Health

Insulin resistance, a hallmark of obesity, leads to compensatory hyperinsulinemia, which promotes:

- Arterial stiffness and endothelial dysfunction.
- Increased oxidative stress, damaging blood vessels.
- Left ventricular remodeling, predisposing to heart failure [6].

Over time, insulin resistance progresses to type 2 diabetes (T2DM), which is associated with an even higher risk of cardiovascular disease, myocardial infarction, and heart failure due to accelerated vascular damage [7].

Atherosclerosis and Endothelial Dysfunction: Evidence from Clinical Studies

Atherosclerosis, once considered a disease of middle-aged adults, begins in childhood, especially in obese individuals. Clinical studies using carotid artery intima-media thickness (CIMT) measurements have shown that obese adolescents already exhibit arterial wall thickening and plaque formation, confirming the early onset of vascular disease [8].

Endothelial dysfunction, a precursor to atherosclerosis, is driven by:

- Oxidative stress
- Chronic inflammation
- Reduced nitric oxide (NO) bioavailability

These factors compromise vascular elasticity, increasing the likelihood of hypertension, stroke, and myocardial infarction later in life [9].

Left Ventricular Hypertrophy (LVH) and Cardiomyopathy

Chronic hypertension and increased cardiac workload lead to left ventricular hypertrophy (LVH) in obese adolescents. LVH is characterized by:

- Increased heart muscle thickness, reducing the heart's ability to pump efficiently.
- Diastolic dysfunction, impairing ventricular relaxation.
- Higher risk of heart failure and arrhythmias [10].

Severe obesity is also linked to obesity-related cardiomyopathy, where fat infiltration of the myocardium contributes to dilated heart chambers, reduced cardiac contractility, and eventual heart failure.

Risk Factors and Comorbidities

The development of cardiovascular disease in adolescents with severe obesity is influenced by genetic, lifestyle, socioeconomic, and physiological factors. Understanding these risk factors is essential for early prevention and targeted interventions.

Genetic Predisposition

Genetic factors play a crucial role in obesity and associated cardiovascular risk. Specific gene polymorphisms in leptin (LEP), adiponectin (ADIPOQ), and melanocortin-4 receptor (MC4R) have been linked to altered metabolism, increased appetite, and obesity-related hypertension [1]. However, genetics alone do not determine cardiovascular risk; environmental and lifestyle factors significantly contribute.

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Sedentary Lifestyle and Dietary Habits

Adolescents today engage in less physical activity due to increased screen time, reduced outdoor play, and a sedentary school environment. Poor dietary habits, including:

- High intake of ultra-processed foods and sugary beverages
- Low consumption of fruits, vegetables, and whole grains
- Excessive calorie intake with inadequate nutrient density

These dietary patterns contribute to obesity, insulin resistance, dyslipidemia, and hypertension, increasing cardiovascular risk [2].

Socioeconomic and Psychological Factors

Children from low-income families often have limited access to healthy foods, safe exercise spaces, and healthcare services. Socioeconomic disparities exacerbate obesity prevalence and related complications [3].

Psychological factors, including stress, depression, and emotional eating, are strongly linked to obesity. Adolescents experiencing bullying or low self-esteem are more likely to develop poor dietary habits and physical inactivity, further increasing cardiovascular risk [4].

Sleep Apnea and Obesity-Related Hypoventilation Syndrome

Obstructive sleep apnea (OSA) is common in severely obese adolescents and is characterized by:

- Repeated airway obstruction during sleep
- Hypoxia (low oxygen levels) and hypercapnia (high carbon dioxide levels)
- Increased sympathetic nervous system activation, contributing to hypertension

Chronic OSA is independently associated with cardiovascular morbidity, including hypertension, arrhythmias, and heart failure [5].

Obesity hypoventilation syndrome (OHS), a more severe condition, results in chronic respiratory failure and right heart strain, significantly increasing the risk of pulmonary hypertension and sudden cardiac events [6].

Role of Gut Microbiota in Obesity and CVD

Recent studies suggest that gut microbiota composition plays a crucial role in obesity-related cardiovascular disease. Dysbiosis (microbial imbalance) leads to:

- Increased intestinal permeability
- Systemic inflammation due to lipopolysaccharides (LPS) from gut bacteria
- Altered lipid metabolism, contributing to atherosclerosis [7].

Certain probiotic interventions and dietary modifications have shown promise in modulating gut microbiota and reducing cardiovascular risk in obese individuals. However, more research is needed to explore targeted microbiome-based therapies for CVD prevention [8].

In summary, cardiovascular risk in adolescents with severe obesity is driven by a complex interplay of genetic, behavioral, socioeconomic, and physiological factors. Identifying and addressing these risk factors through early intervention, lifestyle changes, and medical management is essential in preventing long-term cardiovascular complications.

Screening and Diagnosis of Cardiovascular Risk in Obese Adolescents

Early identification of cardiovascular risk in obese adolescents is essential to prevent long-term complications and initiate timely interventions. Screening involves a combination of clinical assessment, laboratory markers, and imaging techniques to evaluate cardiovascular function and metabolic health [11].

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Clinical and Laboratory Markers for CVD Risk

Routine screening in obese adolescents includes:

- Blood Pressure Measurement: Hypertension is a key marker of cardiovascular risk and should be monitored regularly.
- Fasting Blood Glucose and Insulin Levels: Insulin resistance and hyperglycemia indicate metabolic dysfunction.
- Lipid Profile: Elevated low-density lipoprotein (LDL-C), triglycerides, and reduced high-density lipoprotein (HDL-C) signal dyslipidemia, which increases atherosclerosis risk [12].
- C-reactive Protein (CRP) and Interleukin-6 (IL-6): Indicators of chronic systemic inflammation associated with endothelial dysfunction and cardiovascular risk [13].

Imaging Techniques (Echocardiography, MRI)

Advanced imaging techniques help detect early cardiovascular changes:

- Echocardiography: Assesses left ventricular hypertrophy (LVH), cardiac function, and valvular abnormalities.
- Carotid Intima-Media Thickness (CIMT) Measurement: Identifies early atherosclerotic changes and arterial stiffness.
- Cardiac MRI: Provides detailed visualization of heart structure, fat infiltration, and myocardial fibrosis in obese adolescents with suspected cardiomyopathy [14].

Importance of Early Screening and Risk Stratification

Early screening enables risk stratification based on the severity of metabolic and cardiovascular dysfunction. Adolescents at high risk (e.g., those with multiple metabolic abnormalities) require intensive lifestyle modifications, pharmacological therapy, and possible surgical interventions. Screening programs in schools and primary care settings can facilitate early detection and prevent progression to chronic cardiovascular disease in adulthood [15].

Prevention and Management Strategies

The management of cardiovascular risk in obese adolescents involves multidisciplinary interventions, including lifestyle modifications, pharmacological therapy, surgical options, and public health strategies [16].

Lifestyle Modifications: Diet, Physical Activity, Behavioral Therapy

Lifestyle changes form the first-line approach for managing obesity-related cardiovascular risks.

- Dietary Modifications: Emphasis on a balanced, nutrient-dense diet with reduced saturated fats, refined sugars, and processed foods. A Mediterranean or DASH (Dietary Approaches to Stop Hypertension) diet is often recommended [17].
- Physical Activity: At least 60 minutes of moderate-to-vigorous exercise daily, such as aerobic activities (walking, cycling, swimming) and strength training, helps improve insulin sensitivity, lipid profile, and cardiovascular fitness [18].
- Behavioral Therapy: Cognitive-behavioral therapy (CBT) and motivational counseling help adolescents develop long-term adherence to healthy lifestyle choices and address emotional eating patterns.

Pharmacological Interventions: Metformin, Statins, Antihypertensives

In cases where lifestyle interventions alone are insufficient, pharmacotherapy is considered.

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- Metformin: Primarily used for insulin resistance and type 2 diabetes prevention, metformin lowers hepatic glucose production and improves insulin sensitivity [19].
- Statins: Recommended for adolescents with severe dyslipidemia (LDL-C >160 mg/dL), statins reduce cholesterol levels and slow atherosclerosis progression.
- Antihypertensives: ACE inhibitors and calcium channel blockers may be prescribed for adolescents with persistent hypertension despite lifestyle modifications [20].

Surgical Options: Bariatric Surgery in Adolescents—Risks and Benefits

For adolescents with severe obesity (BMI ≥40 kg/m²) and obesity-related comorbidities, bariatric surgery is an option when conservative treatments fail.

- Common procedures include:
  - Roux-en-Y gastric bypass (RYGB)
  - Sleeve gastrectomy
- Benefits: Significant weight loss, improved insulin sensitivity, lipid profile, and blood pressure control.
- Risks: Nutrient deficiencies, surgical complications, and long-term metabolic effects. Postoperative lifelong dietary and lifestyle modifications are necessary [16].

Community and Public Health Interventions: School Programs, Policy Changes

Effective obesity prevention requires community-wide efforts, including:

- School-based programs: Incorporating physical activity, nutritional education, and healthy meal options in schools can reduce obesity rates and promote heart health.
- Policy changes: Government regulations on marketing unhealthy foods to children, imposing sugar taxes, and improving access to healthy foods can curb adolescent obesity trends.
- Parental and peer support: Encouraging family-based interventions and community engagement fosters sustainable lifestyle changes in adolescents [17].

In conclusion, managing cardiovascular risk in obese adolescents requires an integrated approach involving early screening, lifestyle interventions, targeted pharmacotherapy, and public health strategies to reduce long-term morbidity and improve quality of life.

Future Directions and Research Gaps

Despite significant advancements in understanding the cardiovascular risks associated with adolescent obesity, several research gaps remain. Future studies must focus on long-term outcomes, emerging therapies, genetic influences, and digital health innovations to enhance prevention and management strategies [21].

Need for Long-Term Studies on Adolescent Obesity and CVD Progression

Most existing studies on cardiovascular risk in obese adolescents are cross-sectional or short-term, limiting insights into longitudinal disease progression. There is a need for large-scale cohort studies tracking obese adolescents into adulthood to:

- Identify predictors of cardiovascular complications.
- Assess the effectiveness of early interventions.
- Evaluate long-term morbidity and mortality outcomes.

Such studies would provide critical data for refining screening guidelines and treatment approaches [22].

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Role of Emerging Therapies (e.g., GLP-1 Receptor Agonists)

Pharmacological interventions for obesity are evolving, with GLP-1 receptor agonists (e.g., liraglutide, semaglutide) showing promise in reducing weight and improving cardiovascular risk factors. Future research should explore:

- Long-term safety and efficacy of these agents in adolescents.
- Impact on lipid profiles, insulin resistance, and endothelial function.
- Potential for combination therapies integrating pharmacological and lifestyle interventions [23].

Genetic and Epigenetic Influences on Obesity-Related CVD

Advancements in genomics and epigenetics have highlighted the role of genetic predisposition and environmental interactions in obesity-related cardiovascular disease. Future research should focus on:

- Identifying genetic biomarkers for early risk stratification.
- Understanding epigenetic modifications in response to diet, physical activity, and metabolic changes.
- Exploring personalized medicine approaches for targeted interventions in high-risk adolescents [24].

Digital Health Tools for Monitoring Cardiovascular Risk

The integration of digital health technologies offers new possibilities for obesity and CVD management. Future research should assess:

- The effectiveness of wearable devices and mobile apps in tracking weight, activity levels, and cardiovascular parameters.
- The impact of AI-driven predictive models in identifying at-risk adolescents.
- The role of telemedicine interventions in improving adherence to lifestyle modifications and medical treatments [25].

Addressing these research gaps will enhance our ability to predict, prevent, and manage cardiovascular disease in obese adolescents more effectively.

Conclusion

Adolescent obesity is a major public health crisis with profound implications for cardiovascular health. This review has highlighted the pathophysiological mechanisms, key cardiovascular complications, and the importance of early screening and intervention. The evidence suggests that hypertension, dyslipidemia, insulin resistance, and atherosclerosis begin in adolescence, increasing the risk of premature cardiovascular disease [26].

Early intervention is crucial in preventing long-term complications. Lifestyle modifications, pharmacotherapy, and bariatric surgery can play significant roles in reducing obesity-related cardiovascular risk factors. Additionally, school-based programs and policy-level changes are essential for addressing the root causes of adolescent obesity [27].

Looking ahead, long-term studies, emerging pharmacological therapies, genetic research, and digital health tools will shape future strategies for early detection, personalized treatment, and improved health outcomes. Governments and healthcare providers must work together to strengthen public health initiatives, improve screening programs, and expand access to effective treatment options [28].

With a multifaceted and proactive approach, it is possible to reduce the burden of cardiovascular disease in adolescents with severe obesity, ensuring healthier futures for generations to come.

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