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# CHILDHOOD OBESITY AS A PREDICTOR OF TYPE 2 DIABETES MELLITUS IN ADULTS : A SYSTEMATIC REVIEW

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## Abstract

*The United States of America and other countries all over the world are not the only ones experiencing a growing epidemic of childhood obesity as a major threat to public health. This is a problem that affects countries in all parts of the world. At the moment, one child in the United States out of every three is either overweight or obese. This problem is especially prevalent among young people. Obesity treatments need to be community-based and environment-focused in order to put an end to the epidemic of obesity. As the prevalence of pediatric obesity continues to climb, comorbidities that were once regarded of as "adult" illnesses, such as type 2 diabetes mellitus, hypertension, nonalcoholic fatty liver disease, obstructive sleep apnea, and dyslipidemia, are becoming increasingly common in children. Even a slight gain in weight before puberty is associated with an increased risk of type 2 diabetes and cardiovascular disease later in life; hence, immediate action is required. The presence of insulin in the bloodstream despite a decreased tissue sensitivity to insulin is characteristic of type 2 diabetes. There is a strong correlation between being overweight or obese and developing type 2 diabetes. As a result, the hypothesis that overeating is the root cause of Type 2 Diabetes. Due to muscle and islet -cell insulin resistance, which promotes greater glucagon production, obesity raises the chance of developing type 2 diabetes mellitus in persons who are already genetically susceptible to developing the condition. On the other hand, obesity is not the primary risk factor for developing type 2 diabetes.*

**Katakunci:** *Diabetes Mellitus; Insulin Resistance; Obesity; Body Masss Index; Weight*

## INTRODUCTION

According to statistics provided by the World Health Organization (WHO), more than half of adult population around the globe is overweight or obese. Obesity prevalence is still quickly increasing in many parts of the world, and if current trends continue, it will reach internationally 18% in men and surpass 21% in women by 2025.[1] This would place a significant burden on individuals, societies, and health care systems worldwide. In light of these findings, obesity has been appropriately labeled as a contemporary form of many global epidemic diseases.[2–4]

The United States and other countries across the world are not the only ones facing a growing epidemic of childhood obesity as a major threat to public health. At the present time, one out of every three children living in the United States is either overweight or obese.[5] These situations rarely involve pathologic obesity. Genetic, hormonal, dietary, physical activity, and environmental variables cause most.[6] Obesity prevention strategies have mostly focused on behavioral settings, such as increasing regular physical activity or modifying food. However, impacts have been limited worldwide and have failed to reverse obesity prevalence.[7,8]

To end the obesity epidemic, obesity therapies must be community-based and environment-focused. Comorbidities that were formerly thought of as "adult" disorders, such as type 2 diabetes mellitus, hypertension, nonalcoholic fatty liver disease, obstructive sleep apnea, and dyslipidemia, are becoming more common in children as the prevalence of pediatric obesity rises. Moderate overweight before puberty increases the risk of type 2 diabetes and cardiovascular disease in midlife, thus action is needed now.[9,10] This article provided evidence that a correlation exists between obesity in childhood and an increased risk of developing type 2 diabetes in adulthood.

## METHODS

The methodology of this systematic review was based on the criteria established by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 checklist. The purpose of this systematic review was to assess the association between childhood obesity as a predictor of type 2 diabetes mellitus in adults. The subject matter being examined is the focus of the studies under evaluation. To effectively evaluate existing studies, it is important that these studies meet certain criteria, including: 1) It is important that articles are available online for easy accessibility; 2) It is preferred that articles are written in English; and 3) The systematic review will only consider articles published between 2015 and the present time.

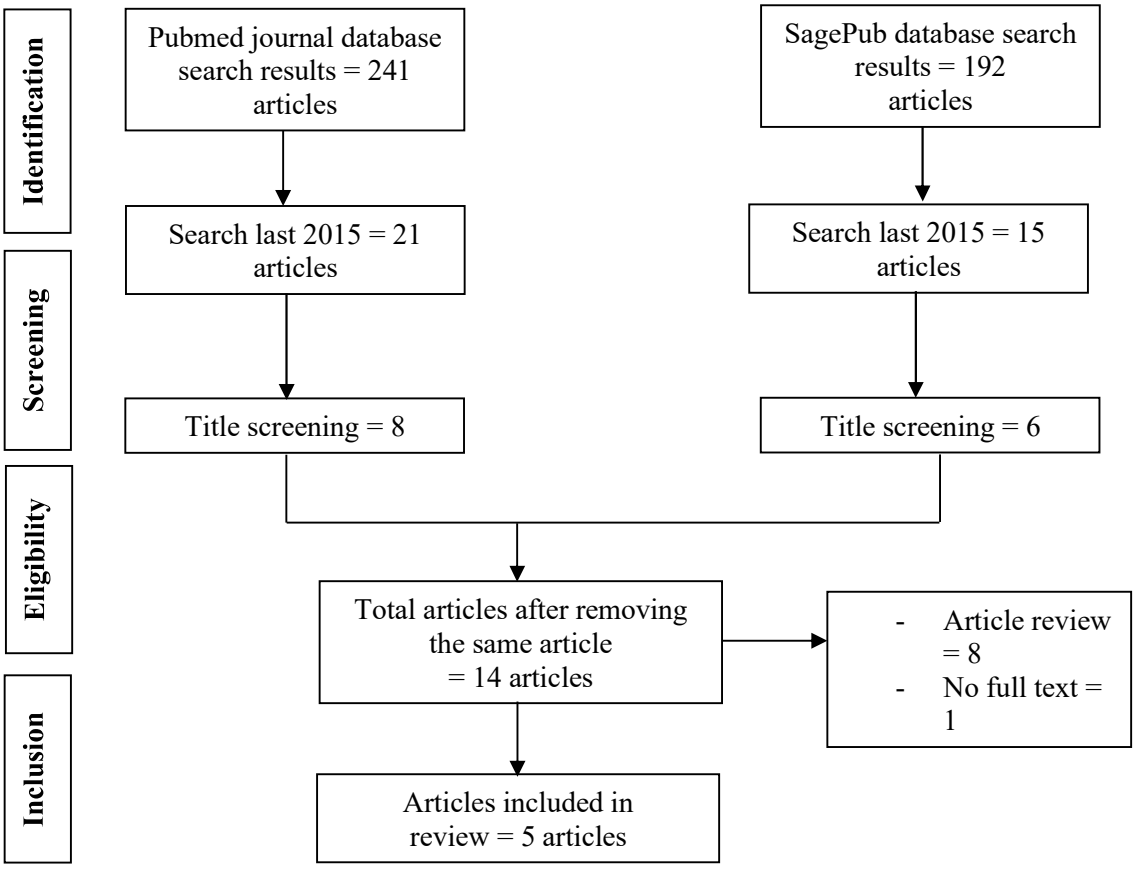


**Figure 1. Article search flowchart**

The search for studies to be included in the systematic review was carried out from May 10th, 2023 using the PubMed and SagePub databases by inputting the words: “childhood obesity” and “type 2 diabetes mellitus”. Where *(("associate"[All*

*Fields] OR "associated"[All Fields] OR "associates"[All Fields] OR "associating"[All Fields] OR "association"[MeSH Terms] OR "association"[All Fields] OR "associations"[All Fields]) AND ("pediatric obesity"[MeSH Terms] OR ("pediatric"[All Fields] AND "obesity"[All Fields]) OR "pediatric obesity"[All Fields] OR ("childhood"[All Fields] AND "obesity"[All Fields]) OR "childhood obesity"[All Fields]) AND ("diabetes mellitus, type 2"[MeSH Terms] OR "type 2 diabetes mellitus"[All Fields]) AND ("adult"[MeSH Terms] OR "adult"[All Fields] OR "adults"[All Fields] OR "adult s"[All Fields])) AND (2015:2023[pdat])* is used as search keywords.

The study's inclusion and exclusion criteria were revised following a thorough review of the literature based on an inspection of the titles and abstracts of previously published research. Only research projects that met all of the requirements were included in the systematic review. The title, author, publication date, country of origin, research design, and variables being researched are just a few of the crucial factors to consider when comparing one research study to another.

The offered content has been presented in a specific format for your attention and critical evaluation. The writers conducted independent appraisals of a selection of research endeavors stated in the titles and abstracts of the publications to determine whether the investigations were eligible for inclusion. The full texts of the studies that meet the criteria for inclusion in the systematic review will then be assessed to determine which publications are eligible for categorical inclusion in the review.

**RESULT**

Hudda, et al (2021)[11] conducted a cohort study. After adjusting for childhood height, increases in FM and weight (per kilogram) among boys aged 10 years were associated with elevated T2D risks at age 50 years of 12% (hazard ratio [HR] = 1.12; 95% confidence intervals [CI] = 1.10-1.14) and 7% (HR = 1.07; 95% CI = 1.05-1.09), respectively, and among girls aged 10 years of 15% (HR = 1.15; 95% CI = 1.13-1.17) and 10% (HR = 1.10; 95% CI = 1.08-1.11), respectively. Among children aged 13 years, increases in FM and weight (per kilogram) were associated with elevated T2D risks at age 50 of 10% (HR = 1.10; 95% CI = 1.09-1.11) and 6% (HR = 1.06; 95% CI = 1.05-1.07) for boys and 10% (HR = 1.10; 95% CI = 1.10-1.11) and 7% (HR = 1.07; 95% CI = 1.06-1.08) for girls.

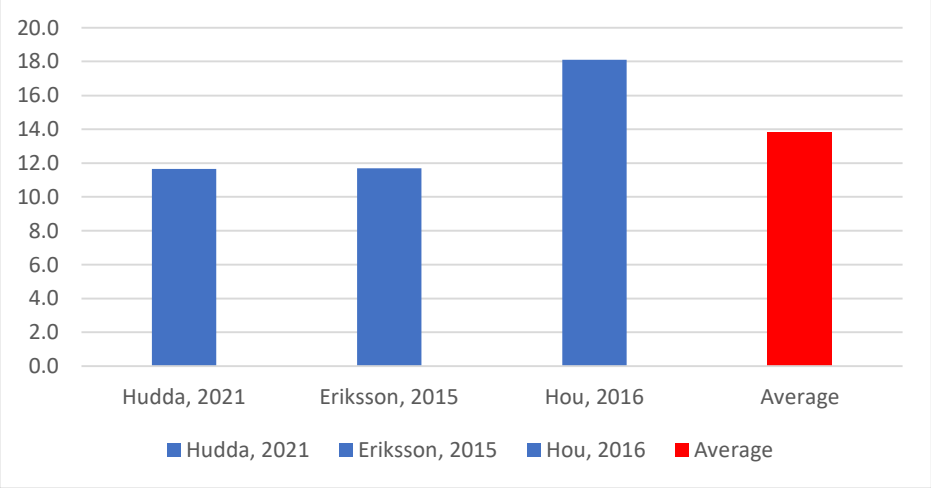


**Figure 2. Percentage of pediatric patients with obesity who develop type 2 DM as adults**

With few exceptions, Zimmermann (2017) showed BMIs below the average were not associated with type 2 diabetes. Positive associations with BMIs above average were stronger in women than in men, stronger in younger birth cohorts, and weakened with increasing age at diagnosis. Women born between 1930 and 1947, 1948 and 1965, and 1966 and 1983 who had an above-average BMI at 13 years (18.2 kg/m2) had hazard ratios (95% confidence intervals) ranging from 2.12 (1.91-2.36) to 2.84 (2.31-3.49) per z score when diagnosed between 30 and 47 years of age. The birth weight had no effect on these associations.[12]

**Table 1. The litelature include in this study**

| Author | Origin | Method | Sample Size | Result |
|---|---|---|---|---|
| Hudda, 2021[11] | Denmark | Retrospective cohort study | 269,913 school-children aged 10 years with 21,896 established adult T2D cases and 261,192 children aged 13 years with 21,530 established adult T2D cases | Independent of childhood height, this cohort study found that a 1-kg increase in childhood FM was more significantly associated with increased adult T2D risk than a 1-kg increase in weight. Information on FM, as opposed to weight-based measures, concentrates on a modifiable component of weight that may be associated with the risk of type 2 diabetes in adults. In an effort to reduce long-term T2D risk, these results support the incorporation of |

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|---|---|---|---|---|
| | | | | childhood FM into adiposity surveillance programs. |
| Zimmermann, 2017[12] | Denmark | Retrospective cohort study | 292,827 individuals, born between 1930 and 1989, were followed in national registers for type 2 diabetes | When a kid has a BMI that is below the average, there is no increased risk of developing type 2 diabetes later in life. However, when a child has a BMI that is above the average, there is a significant increased risk of developing type 2 diabetes in adulthood, which corresponds to increased risks even at levels that are below the international definition of overweight. Although the correlations are stronger in women than in men, birth weight has no bearing on the phenomenon. |
| Petkeviciene, 2015[13] | Lithuania | Retrospective cohort study | 506 patients | While the risk of hypertension, higher triglycerides, and reduced HDL cholesterol is connected more strongly with BMI gain from childhood to adulthood, the risk of metabolic syndrome, hyperglycemia and diabetes, and elevated high-sensitivity CRP may be altered by childhood BMI and skinfold thickness. |
| Eriksson, 2015[14] | Finland | Prospective cohort study | 13,345 individuals | T2D is caused by two different early growth routes. The low amount of fat deposition that occurs in thinness at birth and during infancy leads to subsequent weight gain during development. A shorter length at birth is connected with reduced linear growth, which in adulthood is associated with a lower proportion of body fat but also an increased risk of developing diabetes. |
| Hou, 2016[15] | China | Retrospective cohort study | 3,198 children | Even if it was maintained into maturity, obesity in children was a risk factor for developing diabetes in adulthood. It is essential to have a handle on childhood obesity if one want to forestall diabetes in adulthood. |

Other study with 35 years of follow-up showed men experienced a greater increase in BMI than women. Childhood anthropometric measurements correlate significantly with adult anthropometric values. Weight and BMI measurements had the highest correlation coefficients (r = 0.56 and r = 0.51, respectively, for females; r = 0.45 and r = 0.41, respectively, for boys; P 0.001). In all quintiles of childhood BMI, the mean change in BMI was comparable; however, the prevalence of adult obesity increased significantly with increasing quintiles.[13]

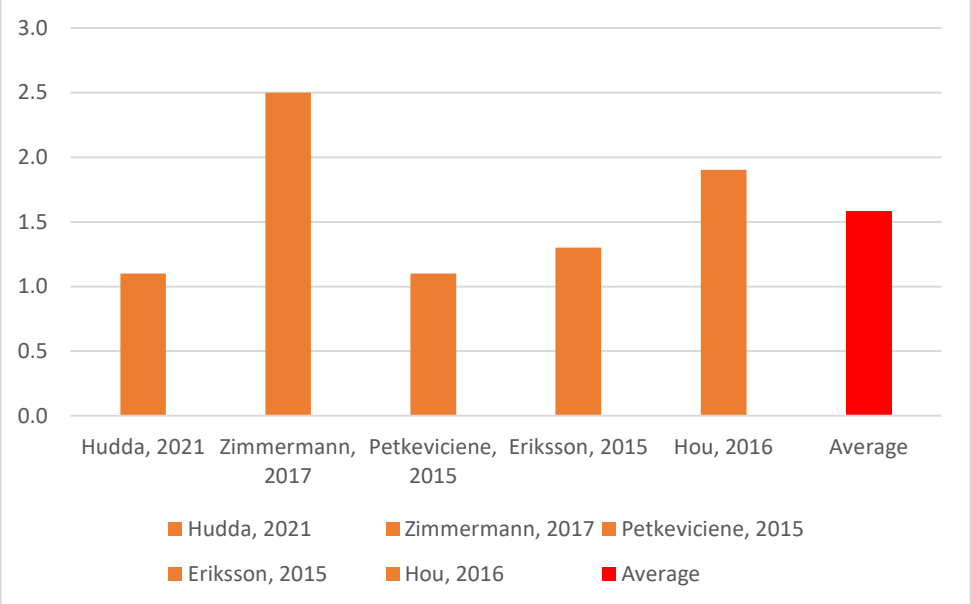


**Figure 3. OR of pediatric patients with obesity who develop type 2 DM as adults**

Regardless of BMI gain from childhood to adulthood, the risk of adult obesity, metabolic syndrome, hyperglycemia or type 2 diabetes, and elevated level of high-sensitivity CRP increased with increasing childhood BMI and skinfold thicknesses. There was no correlation between childhood anthropometric measurements and arterial hypertension,

elevated triglyceride levels, or decreased HDL cholesterol levels. Independent of childhood BMI, the increase in BMI from childhood to maturity was associated with increased odds of all of the above-mentioned risk factors.[13]

Eriksson, et al (2015)[14] showed T2D was linked to two different growth pathways. Both began with low birth weight and BMI. In one case, a persistently low BMI during childhood was followed by a fast increase in BMI. The odds ratio for T2D associated with a one z-score rise in BMI between 2 and 11 years was 1.31 (95% CI = 1.21-1.42, P <0.001) among those with a BMI 11 years above the median value. Low BMI at birth, associated by short length at birth, was followed by low BMI in childhood in the other pathway. Most diabetic women followed this pattern; they acquired T2D at a lower BMI and fat percentage than women with a BMI above the median at 11 years of age.

Other study showed FPG and 2 h PG diagnosed diabetes in obese children (16.2%) was higher than in non-obese children (5.6%) (P<0.001). Compared to non-obesity children (6.9%), obese children (18.1%) had a higher prevalence of diabetes diagnosed by HbA1c. After controlling follow-up age, genders, and lifestyle, those obese only in childhood or only in adulthood did not predict any risk of diabetes diagnosed by blood glucose in adults (OR = 1,90; 95% CI = 0.86-4.19; OR = 1.71; 95% CI = 0.50-5.79, respectively).[15]

Obesity in infancy and adulthood increased the probability of adult blood glucose-diagnosed diabetes (OR = 4,50; 95% CI = 2.22-9.14. After controlling age, sex, and lifestyle (smoking, alcohol, dietary, and sleeping), those obese only in childhood or only in adulthood did not increase the risk of diabetes diagnosed by HbA1c in adults (OR = 1,42; 95% CI = 0.71-2.86; OR = 3.13; 95% CI = 0.83-11.75, respectively). Obesity in childhood and adulthood increased the chance of adult HbA1c-diagnosed diabetes.[15]

**DISCUSSION**

Diabetes mellitus is a condition characterized by chronic hyperglycemia that results in physical injury, physiologic dysfunction, and organ failure, particularly in the eyes, kidneys, nerves, heart, blood vessels, and brain. The specific glucose level definition of diabetes is 8-hour post-fasting blood glucose > 126 mg/dl or 2-hour post-meal blood glucose > 200 mg/dl.[16] Type 2 diabetes occurs when insulin production persists but tissue response to insulin is diminished. Type 2 diabetes is frequently associated with being overweight or obese. Consequently, the notion that gluttony causes Type 2 Diabetes.[17]

Hudda, et al found that a 1-kg increase in childhood FM levels was more strongly linked to adult T2D risk than a 1-kg increase in childhood weight. This was true even after we took height into account. Also, height-adjusted associations for childhood weight given per SD increase were stronger than those for childhood FM, even though the 95% confidence intervals mostly overlapped.[11] Due to the dearth of historic cohorts having information on both childhood body composition and adult T2D diagnoses, previous studies on childhood adiposity and T2D risk have focused on BMI rather than weight, FM, or FFM.[12]

The primary causes of obesity are excessive glucose and insulin. When more glucose (energy) is available in the body than is required for cardiac and skeletal muscle function, it is stored as triglycerides or "fat" in adipocytes. The most common pathway involves the consumption of carbohydrates and proteins, which stimulate an increase in endogenous insulin release, allowing glucose to be utilized for muscle function and stored as fat. Without glucose and insulin, the body is incapable of producing or storing fat.[18]

When elevated insulin levels occur as a result of cardiac and skeletal muscle resistance to the action of insulin, the accumulation of excess fat follows. The greatest tissue in the human body, skeletal muscle is essential for locomotion and metabolism. It is estimated to be responsible for 80% of the glucose disposal stimulated by insulin.[19] Skeletal muscle insulin resistance reduces intracellular glucose and fatty acid transport, which reduces these essential fuels for skeletal and cardiac muscle function. Elevated glucagon increases hepatic glucose production and availability, which stimulates fatty acid release.[20]

This may occur because of α-cell insulin resistance which blunts the normal suppression of glucagon release caused normally by insulin, or because increased lipid levels do not increase mitochondrial ATP production in muscles. In contrast, lean pre-type 2 diabetic subjects experience a delay in the commencement of insulin action, and insulin's capacity to maximally stimulate glucose uptake is significantly reduced. This is because lean pre-type 2 diabetic subjects are at a higher risk of developing type 2 diabetes. Subjects with type 2 diabetes have a decrease in insulin-stimulated leg muscle glucose absorption of around fifty percent during the final hour of an insulin clamp.[20,21]

As a marker of childhood BF and a classification tool for children with overweight or obesity, the body mass index has several limitations. As a measure based on weight, it does not distinguish between FM and FFM, which can vary significantly in individuals with a given BMI. The results of this study indicate that, when compared on a per-kilogram basis, childhood FM was more strongly associated with T2D risk in adulthood than childhood weight, suggesting that childhood FM, rather than weight, may be a more accurate indicator of the influence of childhood adiposity on long-term T2D risk.[21]

The presentation of a per-kilogram increase in juvenile body composition effect sizes has been favored because all of the markers are measured on the same scale. Despite the fact that HRs were greater per SD increase in weight compared to FM outcomes per SD, the SD of weight was nearly double that of FM, resulting in a potentially inflated HR for weight.[21] In this instance, we believe that comparisons of per-kilogram increases in effect sizes of body composition variables would provide a fairer and more robust evaluation of associations with prospective outcomes.[22,23]

## CONCLUSION

Obesity increases the risk of type 2 diabetes mellitus in genetically predisposed individuals due to muscle and islet α-cell insulin resistance, which promotes increased glucagon production. However, obesity is not the primary cause of type 2 diabetes.

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