Pediatric Endocrinology Diabetes and Metabolism
Endokrynologia, Diabetologia i Choroby Przemiany Materii Wieku Rozwojowego

Original paper | Praca oryginalna

Pediatr Endocrinol Diabetes Metab 2022; 28 (4): 274–280
DOI: https://doi.org/10.5114/pedm.2022.121369

redakcja@pediatricendocrinology.pl
www.pediatricendocrinology.pl
www.pteidd.pl

Incidence of hyperglycaemic disorders in children and adolescents with obesity

Stany hiperglikemiczne u dzieci i młodzieży z otyłością

Aneta Chylińska-Frątczak, Arkadiusz Michalak, Anna Baranowska-Jaźwiecka, Beata Mianowska, Agnieszka Szadkowska

Department of Paediatrics, Diabetology, Endocrinology, and Nephrology, Medical University of Lodz, Poland

Abstract

Introduction: The prevalence of obesity in the paediatric population has increased significantly in recent decades. To date, the rarest metabolic disturbance associated with obesity has been the hyperglycaemia, including diabetes.

The aim of the study was to compare the prevalence of hyperglycaemic disorders diagnosed on the basis of (1) the oral glucose tolerance test (OGTT) and (2) the HbA_{1c} value, and to estimate the prevalence of hyperglycaemia in continuous glucose monitoring (CGM) records in adolescents with obesity.

Material and methods: The study included patients aged 9–18 years with obesity (BMI ≥ 95th percentile). The height, body weight, and waist circumference were measured, and the BMI and BMI Z-score were calculated. Sexual maturity was assessed on the Tanner scale. OGTT was performed, and the HbA_{1c} value was measured. Six-day retrospective blinded CGM was performed.

Results: In the group of 143 children (mean age 13.4 years), the severity of obesity positively increased with patients age ($r = 0.36$ and $p < 0.0001$). Abdominal obesity was found in 93.4% of children. Based on OGTT, 18.8% of the subjects had hyperglycaemic disorders; impaired glucose tolerance was the most common one (16.1%). Impaired fasting glucose was found in 4 patients (2.8%), and type 2 diabetes was found in 2. The mean HbA_{1c} was 5.4%. HbA_{1c} values ranged from 5.7 to 6.4% in 20.3% of the patients, and it did not exceed 6.4% in any patient. In 27.6% of patients with HbA_{1c} 5.7–6.4%, abnormalities in OGTT were observed (IGT 17.25%, IFG 6.9%, DM2 3.45%). There was a significant discrepancy between OGTT results and HbA_{1c} in the diagnosis of hyperglycaemic disorders (diagnosis agreement – 69.92%). In CGM 1.4% of results were above 140 mg/dl.

Conclusions: Hyperglycaemic disorders are diagnosed in nearly 20% of children with obesity. However, there are significant discrepancies in the diagnosis of glucose disturbances using OGTT and HbA1c. Concordance in the diagnosis of hyperglycaemic disorders was achieved only in 70% of patients. CGM may be useful in the diagnosis of pre-diabetes in people with obesity.

Key words:
obesity, hyperglycaemic disorders, OGTT, HbA_{1c}, CGM.

Streszczenie

Wprowadzenie: Częstość występowania otyłości w populacji pediatrycznej znacznie wzrosła w ostatnich dziesięcioleciach. Do tej pory najrzadszym zaburzeniem metabolicznym związanym z otyłością była hiperglikemia, w tym cukrzyca.

Celem pracy było porównanie częstości występowania stanów hiperglikemicznych rozpoznawanych na podstawie (1) doustnego testu tolerancji glukozy (OGTT) i (2) stężenia HbA_{1c} oraz ocena częstości występowania hiperglikemii przy użyciu ciągłego monitorowania glikemii (CGM) u młodzieży z otyłością.

Materiał i metody: Badaniem objęto pacjentów w wieku 9–18 lat z otyłością (BMI ≥ 95. percentyl). Zmierzono wzrost, masę ciała, obwód talii; obliczono BMI i BMI Z-score; dojrzałość płciową oceniono w skali Tannera. Przeprowadzono OGTT; zmierzono stężenie HbA_{1c}. Wykonano 6-dniowy retrospektywny, zaślepiony zapis CGM.

Wyniki: W grupie 143 dzieci (średnia wieku 13,4 roku) nasilenie otyłości narastało z wiekiem pacjentów ($r = 0,36$ i $p < 0,0001$). Otyłość brzuszną stwierdzono u 93,4% dzieci. Na podstawie OGTT u 18,8% badanych stwierdzono stany hiperglikemiczne, najczęściej upośledzoną tolerancję glukozy (16,1%). Nieprawidłową glikemię na czczo stwierdzono u 4 chorych (2,8%), a cukrzycę typu 2 u 2 chorych. Średnia HbA_{1c} wyniosła 5,4%. Wartości HbA_{1c} wahały się od 5,7 do 6,4% u 20,3% pacjentów; u żadnego pacjenta poziom HbA_{1c} nie przekroczył 6,4%. U 27,6% pacjentów z HbA_{1c} 5,7–6,4% zaobserwowano nieprawidłowości w OGTT (IGT 17,25%, IFG 6,9%, DM2 3,45%). Wystąpiła istotna rozbieżność między wynikami OGTT a HbA_{1c} w diagnostyce stanów hiperglikemicznych (zgodność diagnoz – 69,92%). W CGM 1,4% odczytów było powyżej 140 mg/dl.

Aneta Chylińska-Frątczak
Department of Paediatrics, Diabetology, Endocrinology, and Nephrology, Medical University of Lodz, Sporna 36/50, 92-117 Lodz, Poland
tel.+48 42 61 77 750,
e-mail: anetamichal@wp.pl

Received: 6.05.2022
Accepted: 2.08.2022
Conflict of interests: none declared.

Wnioski: Stany hiperglikemiczne rozpoznaje się u blisko 20% dzieci z otyłością. Istnieją jednak istotne rozbieżności w diagnostyce zaburzeń glikemii za pomocą OGTT i HbA_{1c}. Zgodność w diagnostyce stanów hiperglikemicznych osiągnięto tylko u 70% pacjentów. CGM może być przydatne w diagnostyce stanu przedcukrzycowego u osób z otyłością.

Słowa kluczowe:
otyłość, zaburzenia hiperglikemiczne, OGTT, HbA_{1c}, CGM.

Introduction

Obesity is a growing problem among children and adolescents worldwide. According to WHO data, currently 6% of girls and 8% of boys are obese (124 million in 2016), which is a dramatic increase compared to 1975, when the problem affected 1% of children. Over 340 million children and adolescents aged 5–19 were overweight or obese in 2016; 18% of girls and 19% of boys were overweight in 2016 [1]. In Poland, according to the OLAF study (PL0080) conducted in 2007–2009, more than 18% of boys and over 14% of girls were overweight; the prevalence of overweight or obesity by age and sex ranged from 9.1% of girls aged 16 years to 22.4% of boys aged 12 years [2]. The prevalence of obesity increased with age. Based on a study of Polish overweight and obese children aged 5–18 years, it was established that 36.6% of the patients were overweight or obese at the age of 2 years, 73.9% at the age of 4, and 84% at the age of 6 [3].

Excess body weight leads to lipid metabolism disorders, arterial hypertension, and hyperglycaemic disorders (diabetes or other abnormal glucose metabolism states, i.e. "prediabetes", which, according to ADA, includes (1) impaired fasting glucose (IFG), (2) impaired glucose tolerance, IGT, and (3) increased HbA_{1c} (5.7–6.4%) [4]. The coexistence of these disorders with obesity is referred to as metabolic syndrome, which is associated with more frequent development of atherosclerotic cardiovascular diseases [5]. The incidence of hyperglycaemic states is increasing worldwide [6] . In 2021 the International Diabetes Federation (IDF) estimated the global impaired glucose tolerance (IGT) prevalence at 10.6% and IFG prevalence at 6.2% – in both men and women. The majority of individuals with IGT reside in low-income countries (12.7%), lower- to middle- (10%), and high-income countries (10.4%). The prevalence of IFG in 2021 was similar across high-, middle-, and low-income countries (5.7–5.8%). The Western Pacific regions have the highest IGT prevalence (12.9%), and the South-East Asia region has the lowest prevalence (5.4%). South and Central America have the highest IFG prevalence (10%), and the Western Pacific has the lowest prevalence (2.5%) [7]. Until recently, hyperglycaemic conditions were least frequently diagnosed in Caucasian children. In the American population, among adolescents with overweight and obesity, dysglycaemia was diagnosed in 32.7% of obese children and in 23.6% of overweight children [8]. IDF projections indicate that by 2045 the number of adults with IGT will be 730 million worldwide, corresponding to 11.4% of the world's adult population. IGT responding to 441 million adults and 6.9% of the global adult population [7]. The natural course of carbohydrate metabolism disorders depends on the degree of obesity, its duration, the amount of visceral adipose tissue, and positive family history. Initially, only insulin resistance is observed with compensating hyperinsulinaemia. Along with insulin secretion impairment, impaired glucose tolerance and/or impaired fasting glucose develops. The next stage is diabetes.

According to the Diabetes Poland society, it is recommended that people be screened from risk groups for hyperglycaemic disorders because more than half of the people with diabetes have no symptoms of hyperglycaemia at the disease diagnosis. Regardless of age, screening should be performed in people at risk, including those who are obese [9]. Fasting blood glucose is the most commonly performed screening test, but this test cannot detect impaired glucose tolerance. For this reason, an oral glucose tolerance test (OGTT) is performed. According to the American Diabetes Association, hyperglycaemic disorders, including prediabetes, can be diagnosed based on HbA_{1c} measurement [10]. The Diabetes Poland society has used the HbA_{1c}-based criterion of diabetes diagnosis ($HbA_{1c} \geq 6.5\%$) since 2021.

Both OGTT and HbA_{1c} are flawed in diagnosing hyperglycaemic disorders. Low reproducibility of results based on OGTT has been reported, and the HbA_{1c} value reflecting average glycaemia over the past 3 months is affected by variability in erythrocyte formation and longevity, glycation disorders, haemoglobin disorders, and methods of HbA_{1c} measurement.

Lately, continuous glucose monitoring (CGM) systems have been considered useful in the diagnosis of hyperglycaemia disturbances. Currently, there are no criteria for diagnosing hyperglycaemic diseases on the basis of CGM results, although such research has been extensively carried out among cystic fibrosis patients [10].

Glucose metabolism disturbances present at the stage of prediabetes increase the risk of cardiovascular disease and reduce life expectancy [1, 11]. Younger patients are particularly at risk because their naturally expected lifespan is long. For this reason, hyperglycaemic disturbances should be sought for in high-risk children, including those with obesity [11]. The question arises whether both diagnostic methods (OGTT or HbA_{1c}) similarly allow the diagnosis of the disorders.

The aim of this study was to compare the prevalence of hyperglycaemic disorders diagnosed based on oral glucose tolerance test (OGTT) and by HbA_{1c}, and to estimate the prevalence of hyperglycaemias in continuous glucose monitoring in adolescents with obesity.

Material and methods

The study protocol was approved by the Bioethics Committee at the Medical University of Lodz, No. RNN/224/15/KE. The study included patients with obesity hospitalized between 2013 and 2016 at the Department of Paediatrics, Endocrinology, Dia-

betology, and Nephrology, Central University Hospital in Lodz. Children aged 9–18 years, with BMI ≥ 95th percentile according to OLAF calculator http://olaf.czd.pl/, whose parents consented to their participation in the study were included. Patients with acute inflammatory disorders, concomitant chronic diseases, or secondary causes of obesity (genetic, endocrinopathy) were excluded. Medical examination with assessment of nutritional status (based on anthropometric measures) and puberty (according to the Tanner staging) was performed. The following anthropometric measurements were performed: height (with an accuracy of 0.5 cm), body weight (with an accuracy of 0.1 kg), and waist circumference (with an accuracy of 0.1 cm using a standard measuring tape). The obtained results were presented as absolute and percentile values. The body mass index (BMI) was calculated using the formula weight [kg]/height^2 [m] and expressed as BMI z-score (obtained data were related to the current population reference values from the OLAF study [12]). A 2-hour OGTT was performed with assessment of blood glucose concentration at selected time points (0', 15,' 30', 60', 90', and 120'). The HbA_{1c} concentration was measured using high-performance liquid chromatography (HPLC) (Bio-Rad Laboratories GmbH, Munich, Germany). Blinded, 6-day continuous glucose monitoring (CGM) reports were recorded using an iPro CGM device (Medtronic MiniMed).

Table I. Characteristics of the group

Parameters	Number of patients with available data	Mean ±SD
Age at study (years)	143	13.4 ±2.5
BMI (kg/m^2)	143	30.4 ±4.4
BMI Z-score	143	2.2 ±0.4
Waist circumference [cm]	122	96.0 ±10.5
Waist-height ratio	122	0,6 ±0,1
		n (%)
Abdominal obesity (WC > 90th percentile)	137	128 (93.4%)
Sexual maturity stage	143	I – 20 (14%) II – 35 (24.5%) III – 19 (13.3%) IV – 22 (15.4%) V – 47 (32.9%)

WhtR – waist-height ratio

Table II. Prevalence of hyperglycaemic disorders diagnosed based on OGTT in children and adolescents with obesity (n = 26)

Hyperglycaemic disorders	*n* (%)
Impaired fasting glucose (IFG)	4 (2.8%)
Isolated impaired fasting glucose	1 (0.7%)
Impaired glucose tolerance (IGT)	23 (16.1%)
Isolated impaired glucose tolerance	20 (14%)
Both IFG and IGT in a patient	3 (2.1%)
Diabetes	2 (1.4%)
Total	26 (18.8%)

Nominal variables were summarized as numbers and percentages (n, %) and compared between the groups with the χ^2 or Fisher's test according to the sample size. Continuous characteristics were presented as means ± standard deviation. Distribution of continuous variables was assessed with the Shapiro-Wilk test. Afterwards, the comparisons between the groups were performed with *t*-tests for independent variables. Correlations were assessed using Pearson`s correlation coefficient following largely normal distributions of data. Concordance between OGTT results and HbA_{1c} for detecting glucose tolerance abnormalities was measured with Cohen's k. For all the tests, an α threshold of 0.05 was set for declaring significance. All calculations were performed using Statistica 13.1 (Tibco).

Results

The study group included 151 patients with obesity. Eight individuals without current HbA_{1c} values were excluded. The final analysis included 143 patients (65 girls and 78 boys) with a mean BMI of 30.4 kg/m^2 and BMI Z-score of 2.2. Detailed characteristics of the group are presented in Table I.

The severity of obesity (BMI z-score) positively increased with patients age (r = 0.36 and $p < 0.0001$).

Girls presented higher sexual maturity than boys. The median of the Tanner stage for girls was 4 (25–75%: 2 to 5) and for boys it was 3 (25–75%: 2 to 4; p = 0.007) at similar ages (13.6 ±2.4 years vs. 13.3 ±2.6 years; p = 0.383). After adjusting for the Tanner stage, no differences in BMI z-score were observed between girls and boys (p = 0.110).

Abdominal obesity was diagnosed in 93.4% of the patients. No difference was found between genders (92.3% for boys vs. 90.8% for girls, p = 0.741).

Abnormal OGTT results were observed in 26 (18.8%) children; in 2 of them type 2 diabetes (DM2) was diagnosed (Table II). No abnormalities in OGTT were found in prepubertal patients. Both the DM2 patients were at Tanner stage 5.

No statistically significant correlation was found between BMI Z-score and blood glucose level at any of the OGTT time points. There were no differences in the prevalence of hyperglycaemic disorders between genders – based on OGTT, 15 (19.2%) boys vs. 11 (16.9%) girls (p = 0.722). There was no

Table III. Characteristics and comparison of patients whose classification of hyperglycaemic disorders based on OGTT and HbA_{1c} criteria were discordant ($n = 43$)

	HS according to OGTT but not HbA_{1c} ($n = 20$)		HS according to HbA_{1c} but not OGTT ($n = 23$)		
Continuous characteristics					
Hyperglycaemic disorders	*N* with available data	Mean ±SD	*N* with available data	Mean ±SD	*p*
Age [years]	20	13.2 ±2.6	23	14.3 ±2.4	0.169
BMI Z-score	20	2.3 ±0.4	23	2.4 ±0.4	0.468
Waist circumference [cm]	19	99.9 ±11.5	17	99.6±12.1	0.939
Waist-height ratio	19	0.6 ±0.1	17	0.6 ±0.1	0.665
Categorical characteristics					
	n (%)		*n* (%)		*p*
Gender – male	12 (60%)	13 (52%)	1.0000	2 (1.4%)	2 (1.4%)
Abdominal obesity	20 (100%)	20 (87%)	0.2359	26 (18.8%)	26 (18.8%)

HS – hyperglycaemic state; OGTT – oral glucose tolerance test

significant difference in the incidence of hyperglycaemic disorders between patients with and without abdominal obesity.

The mean HbA_{1c} value was 5.4 ±0.3%. There was no correlation between HbA_{1c} and BMI Z-score ($r = 0.05$, $p = 0.549$).

In none of the patients HbA_{1c} was > 6.5%. HbA_{1c} in range 5.7 to 6.4% was found in 29 children (20,3%), with no difference in percentages between boys and girls; 16 (20.5%) vs. 13 (20%), respectively ($p = 0.939$).

In 2 patients in whom DM2 was diagnosed based on OGTT, values of HbA_{1c} were 6.2% and 5.1%.

A significant discrepancy was demonstrated between OGTT and HbA_{1c} results in diagnosing hyperglycaemic disorders. Among children with HbA_{1c} between 5.7 and 6.4%, abnormal OGTT results were observed in 8 (27.6%) (including IGT in 5, IGT in 2, and type 2 diabetes in one patient). Concordant glycaemic states diagnosed based on both these tests were found in 99 patients (69.2%) ($p < 0.001$).

Patients whose glycaemic status was classified differently based on OGTT vs. HbA_{1c} ($n = 43$) did not differ significantly in terms of the analysed clinical parameters (Table III). Patients who were differently classified as suffering from hyperglycaemic states ($n = 43$) according to the OGTT and HbA_{1c} criteria did not differ significantly in terms of the analysed clinical parameters (Table III).

The CGM was performed in 46 patients who did not significantly differ from the other patients in terms of age, BMI Z-score, HbA_{1c}, and the incidence of hyperglycaemic states (diagnosed according to HbA_{1c} or OGTT). The mean glucose level in CGM records was 101.2 mg/dl, 98.5% of glucose readings ranged from 70 to 140 mg/dl, and 1% were over 140 mg/dl. Glucose values below 70 mg/dl constituted 0.5% of all the readings. The mean glucose level was 96.2 mg/dl at night (from midnight till 6 a.m.) and 102.9 mg/dl during the daytime.

Fasting glucose levels significantly correlated with the CGM 24-h mean glucose levels ($R = 0.27$, $p = 0.067$), mean glucose levels at night ($R = 0.43$, $p = 0.003$), 24-h lowest glucose levels ($R = 0.30$, $p = 0.046$), the lowest glucose levels during the daytime ($R = 0.30$, $p = 0.040$), and lowest glucose levels at night ($R = 0.37$, $p = 0.011$). Blood glucose level at the 120' OGTT timepoint significantly correlated with the CGM mean glucose level ($R = 0.36$, $p = 0.015$), the mean glucose level during the daytime ($R = 0.40$, $p = 0.006$), and the 24-h highest glucose level ($R = 0.49$, $p = 0.001$).Positive correlation was found between HbA_{1c} values and mean CGM night-time glucose levels ($R = 0.29$, $p = 0.046$).

Based on CGM analysis short episodes of glucose levels < 70 mg/dl during daytime were found in 14 children (30%), including values < 54 mg/dl in one patient. No abnormalities in OGTT were found in any of these patients, and 4 of them had HbA_{1c} values between 5.7 and 6.4% (Supplementary Table I).

CGM values differed between patients with prediabetes ($n = 5$, IGT and/or IFG) and patients without hyperglycaemia at 0 min and 120 min of OGTT ($n = 41$) only in terms of mean glucose at night (102.2 mg/dl vs. 95.5 mg/dl, respectively; $p = 0.032$) and the lowest blood glucose detected over 24 h (80 mg/dl vs. 70.4 mg/dl, respectively; $p = 0.040$).

Discussion

Based on our results, hyperglycaemic disorders were diagnosed based on OGTT in every fifth child with obesity.

The OGTT is the principal diagnostic tool recommended by the WHO to diagnose hyperglycaemic disorders [13]. In our study group impaired glucose tolerance was the most commonly observed disturbance. Similar results were received by other researchers. In an Italian study carried out on 510 obese children aged 3–18 years, IGT was observed in 11.2% of the subjects (most often in adolescents – 14.8%) and type 2 diabetes in 2 teenagers (0.4%) [14]. In a Montenegrin population, IGT was diagnosed in 19.04% of obese patients and IFG in 4.76% [15]. Differences in IFG and IGT prevalence depend on race. A New Zealand review of studies found a higher prevalence of IFG in Caucasians, while both IGT and a combination of IFG and IGT were more common in Asian populations [16]. In a US study, IGT was found in 25% of obese children aged 4–10 years and in 21% of children aged 11–18 years. Type 2 diabetes was diagnosed in 4% of the subjects [17]. In a Polish study published in 2014, IGT was diagnosed in 4.5% of the 10-16-year-old group and in 3.8% of the group > 16 years of age. IFG was observed in 0.8% of subjects aged 10–16 years and in 1.9% of those aged > 16 years, while DM2 was diagnosed in 3 patients aged 10-16 years (2.3%) [5]. In this study IFG was diagnosed less frequently than IGT, which was also confirmed in the an US study quoted above (below 0.08%) and in Dutch research by Groot (IFG in 1.37% of the subjects) [17, 18]. That may be caused by the fact that usually, at the beginning, prandial impaired insulin secretion occurs, which is later followed by impaired basal insulin secretion.

Hyperglycaemic disturbances in adolescents may be transitory, even in individuals with initial HbA_{1c} values in the range diagnostic for diabetes (> 6.5%) [19].

According to the Diabetes Poland 2021 recommendations, the prediabetic state (IFG and/or IGT) is an indication for lifestyle modification, i.e. striving to achieve permanent body mass reduction, increasing physical activity, as well as considering metformin administration [9].

A study among 79 obese children with IGT demonstrated that in 66% of them glycaemia normalized at one-year follow-up with contributory factors being the following: lower body mass, lower HbA_{1c} concentration, lower blood glucose values in a 2-hour OGTT test, as well as body mass reduction and later puberty over the follow-up period [20]. In the ADA recommendations, the highest efficacy in primary prevention was demonstrated in individuals with IGT with or without accompanying IFG rather than in those with isolated IFG or a prediabetic state defined according to HbA_{1c} criteria [10].

Both puberty and pregnancy are probably critical periods in the development of hyperglycaemia disturbances in adolescents. At those times, increased tissue resistance to insulin occurs, leading to hyperinsulinaemia. Tissue sensitivity to insulin increases again after puberty. Thus, the type 2 diabetes peak coincides with sexual maturity Tanner stages 2–4 [21]. In our study, we found only 2 cases of type 2 diabetes concerning boys aged approximately 17 years at Tanner stage 5. The other cases of hyperglycaemic states diagnosed based on OGTT were observed in our study most commonly at Tanner stages 2 and 5; they were not diagnosed in children before puberty.

OGTT requires appropriate patient preparation, fasting, staying in the laboratory/outpatient clinic for 2 hours, and at least 2 venous blood collections. Children sometimes vomit after drinking glucose solution used for OGTT, which necessitates the test to be discontinued and repeated another day. Therefore, it is quite difficult to monitor the majority of patients who are at risk for hyperglycaemic disorders, including children with obesity, with the use of OGTT. What is more, research results indicate rather low repeatability of OGTT results [22]. Thus, other diagnostic methods to identify hyperglycaemic disorders have been introduced.

In 2010, the American Diabetes Association added HbA_{1c} to diagnose hyperglycaemic disorders defining HbA_{1c} 5.7–6.4% as prediabetes and $HbA_{1c} \geq 6.5\%$ as diabetes [23]. This parameter has gained increasing popularity in other countries too. In 2021 Diabetes Poland also included $HbA_{1c} \geq 6.5\%$ as a criterion to diagnose diabetes in its national recommendations [9].

As described by Herman and Fajans, there are several pros to use HbA_{1c} to diagnose diabetes: 1) no need for the patient to be fasting before blood sample collection; 2) HbA_{1c} concentration is much more stable than glucose concentration in a collected sample; 3) HbA_{1c} determination is more repeatable than blood glucose measurement at 120 minutes in OGTT; and 4) HbA_{1c} is not affected by sudden blood glucose fluctuations caused by stress or acute disease. However, the authors draw attention to limitations of the method, namely the impact of anaemia, hypertriglyceridaemia, and liver and kidney diseases on HbA_{1c} concentration. Lower HbA_{1c} concentrations typically occur in the course of those diseases. Hence, the authors propose joint application of HbA_{1c} percentages and plasma glucose concentrations in diabetes diagnosis, particularly in individuals with comorbidities [24].

The latest ADA standards (2021) recommend screening tests for DM2 or prediabetes in asymptomatic children and adolescents after the onset of puberty or after 10 years of age (depending on which occurs earlier), who are overweight or obese, and have one or more additional DM2 risk factors. According to the ADA, fasting blood glucose, blood glucose at 120 minutes of OGTT, and HbA_{1c} are equally appropriate as screening and diagnostic tests for both prediabetes and diabetes, in individuals at a seemingly low risk with a chance fasting glucose test, as well as in individuals with diabetes risk factors and asymptomatic patients [10]. It should be noted, however, that the tests do not necessarily detect diabetes in the same individuals.

Love-Osborne demonstrated that the ease of HbA_{1c} use may improve screening testing for type 2 diabetes among adolescents in primary healthcare [25].

We found significantly discordant results when using 2 diagnostic methods, OGTT and HbA_{1c}. Concordant diagnoses were received in fewer than 70% of patients. A Korean study of 190 obese children confirmed DM in the OGTT study in 83.3% of people with $HbA_{1c} \geq 6.5\%$. Conversely, 12.5% of people with DM

diagnosed with OGTT had HbA_{1c} < 6.5%. HbA_{1c} levels of 6.15% have also been proposed as the optimal cut-off point for predicting diabetes in children [26]. In turn, a study by Chan it was shown that HbA_{1c} and OGTT are equally useful screening tests for hyperglycaemia disturbances in obese adolescents [27].

A question arises of which prediabetes criterion will better stratify patients in terms of the diabetes development risk and long-term complications of hyperglycaemia [28]. The annual risk of diabetes in a person with IFG is almost 5 times higher than in an individual with normal glucose tolerance, whereas it is 6 times higher in a person with IGT. If IFG is accompanied by IGT, the annual risk of diabetes becomes 12 times as high as in healthy people [29]. According to US researchers, children with HbA_{1c} values within prediabetes range (6.0–6.4%) are at a higher risk of type 2 diabetes development than those with HbA_{1c} values of 5.7–5.9% [8].

Taking the discrepancies into account, other diagnostic methods may be considered. The continuous glucose monitoring (CGM) system is a relatively novel technology enabling frequent glucose measurements without the need to puncture the skin. Currently, parameters received on the basis of CGM have been approved by international experts for assessing glucose control in diabetic patients.

A question arises of whether CGM may be more effective to recognize hyperglycaemic disorders in obese individuals compared to HbA_{1c} and OGTT. The results of some studies indicate that CGM use in prediabetes diagnosis in high-risk groups, including adults and adolescents with obesity (especially with positive family history of type 2 diabetes), gestational diabetes, cystic fibrosis, polycystic ovary syndrome, acute coronary syndrome, and after kidney transplantation, is worth considering in diagnosing hyperglycaemia [30].

According to Finnish research, glucose levels measured in CGM and capillary glucose self-checks are useful in hyperglycaemia detection at the preclinical stage of type 1 diabetes. Elevated blood glucose levels at night are common in that group [31]. A group of Finnish and Italian researchers assessed CGM-based glycaemic variability indicators to show high accuracy in categorizing healthy and diabetic individuals, but slightly lower in dividing patients into groups with impaired glucose tolerance (IGT) and type 2 diabetes (DM2) [32]. Chan *et al.* proved that prediabetic individuals had considerably higher mean glucose levels, maximum glucose levels, areas under curve (AUC), and time spent in the range above glucose 140 mg/dl in CGM compared to adolescents with normal HbA_{1c} or OGTT [27]. El Awwa *et al*. assessed 72-hour CGM, OGTT, HOMA, and QUICKY among 13 teenagers with obesity. OGTT revealed 3 cases (23%) of IFG, 4 cases (30%) of IGT, and no case of diabetes. When using CGM, IFG was detected in 4 cases, IGT in 9 cases, and diabetes in one subject. No hyperglycaemia was detected using HbA_{1c} [33]. In our study only 1% of readings exceeded 140 mg/dl. Compared to subjects with normoglycaemia, in OGTT patients diagnosed as having prediabetes based on OGTT, CGM records showed only higher mean glucose levels at night, AUC at night, and the lowest glucose values over 24 hours compared to patients with normoglycaemia. But we should underline that our study and that of El Awwa included small numbers of subjects with CGM recordings, which is a limitation of both.

Conclusions

Hyperglycaemic disorders were diagnosed in almost 20% of children with obesity. Considerable discrepancies occurred in diagnosing hyperglycaemic states based on OGTT or HbA_{1c}. Concordance in hyperglycaemic state diagnoses based on these 2 tools was confirmed in only 70% of patients. In the future, CGM may find a place in the diagnosis of pre-diabetes in people with obesity.

References

1. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight.
2. Kułaga Z, Litwin M, Tkaczyk M, et al. Polish 2010 growth references for school-aged children and adolescents. Eur J Pediatr 2011; 170: 599–609. doi:10.1007/s00431-010-1329-x
3. Majcher A, Czerwonogrodzka-Senczyna A, Kądziela K, et al. Development of obesity from childhood to adolescents. Pediatr Endocrinol Diabetes Metab 2021; 27: 70–75. doi: 10.5114/pedm.2021.105297
4. American Diabetes Association Professional Practice Committee. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes – 2022. Diabetes Care 2022; 45 (Suppl 1): S17–S38. doi: 10.2337/dc22-S002
5. Skoczeń M, Radwański K, Chrzanowska J, et al. Carbohydrate and lipid metabolism disorders in children with simple obesity accordingto age and degree of obesity. Pediatr Endocrinol 2014; 13: 27–36. doi: 10.18544/EP-01.13.04.1500
6. Echouffo-Tcheugui JB, Selvin E. Prediabetes and What It Means: The Epidemiological Evidence. Annu Rev Public Health 2021; 42: 59–77. doi: 10.1146/annurev-publhealth-090419-102644
7. https://diabetesatlas.org/atlas/tenth-edition.
8. Love-Osborne KA, Sheeder JL, Nadeau KJ, et al. Longitudinal follow up of dysglycemia in overweight and obese pediatric patients: Love-Osborne et al. Pediatr Diabetes 2018; 19: 199–204. doi: 10.1111/pedi.12570
9. Guidelines on the management of patients with diabetes. A position of Diabetes Poland. 2022; 1–134.
10. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes – 2021. Diabetes Care. 2021; 44 (Suppl 1): S15–S33. doi: 10.2337/dc21-S002
11. Cruz ML, Shaibi GQ, Weigensberg MJ, et al. Pediatric Obesity and Insulin Resistance: Chronic Disease Risk and Implications for Treatment and Prevention Beyond Body Weight Modification. Annu Rev Nutr 2005; 25: 435–468. doi: 10.1146/annurev.nutr.25.050304.092625

12. Kułaga Z, Różdżyńska-Świątkowska A, Palczewska I, et al.; Grupa Badaczy OLAF. Siatki centylowe wysokości, masy ciała i wskaźnika masy ciała dzieci i młodzieży w Polsce – wyniki badania OLAF. Stand Med Pediatr. Published online 2010; 690-700.
13. World Health Organization, International Diabetes Federation. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia: report of a WHO/IDF consultation. Published online 2006. Accessed March 28, 2022. Available at: https://apps.who.int/iris/handle/10665/43588
14. Brufani C, Ciampalini P, Grossi A, et al. Glucose tolerance status in 510 children and adolescents attending an obesity clinic in Central Italy. Pediatr Diabetes. 2010; 11: 47–54. doi:10.1111/j.1399-5448.2009.00527.x
15. Rakočević L. Incidence of Cardiovascular Risk Factors in Obese Children. Acta Clin Croat 2016; 55: 407–413. doi:10.20471/acc.2016.55.03.09
16. Yip W, Sequeira I, Plank L, et al. Prevalence of Pre-Diabetes across Ethnicities: A Review of Impaired Fasting Glucose (IFG) and Impaired Glucose Tolerance (IGT) for Classification of Dysglycaemia. Nutrients 2017; 9: 1273. doi: 10.3390/nu9111273
17. Sinha R, Fisch G, Teague B, et al. Prevalence of Impaired Glucose Tolerance among Children and Adolescents with Marked Obesity. N Engl J Med 2002; 346: 802–810. doi: 10.1056/NEJMoa012578
18. Groot CJ de, Grond J van der, Delgado Y, et al. High predictability of impaired glucose tolerance by combining cardiometabolic screening parameters in obese children. J Pediatr Endocrinol Metab. 2017; 30: 189–196. doi: 10.1515/jpem-2016-0289
19. Sallar A, Dagogo-Jack S. Regression from prediabetes to normal glucose regulation: State of the science. Exp Biol Med. 2020; 245: 889–896. doi: 10.1177/1535370220915644
20. Kleber M, Lass N, Papcke S, et al. One-year follow-up of untreated obese white children and adolescents with impaired glucose tolerance: high conversion rate to normal glucose tolerance: Follow-up of children with impaired glucose tolerance. Diabet Med 2010; 27: 516–521. doi: 10.1111/j.1464-5491.2010.02991.x
21. American Diabetes Association. 13. Children and Adolescents: Standards of Medical Care in Diabetes—2020. Diabetes Care 2020; 43 (Suppl. 1): S163–S182. doi: 10.2337/dc20-S013
22. Hudak S, Huber P, Lamprinou A, et al. Reproducibility and discrimination of different indices of insulin sensitivity and insulin secretion. Atkin SL, ed. PLOS ONE 2021; 16: e0258476. doi: 10.1371/journal.pone.0258476
23. Zinman B, Gerich J, Buse JB, et al. American Diabetes Association. Standards of medical care in diabetes-2010. Diabetes Care 2010; 33: 692–692.
24. Herman WH, Fajans SS. Hemoglobin A1c for the diagnosis of diabetes: practical considerations. Pol Arch Med Wewn 2010; 120: 37–40.
25. Love-Osborne KA, Sheeder J, Svircev A, et al. Use of glycosylated hemoglobin increases diabetes screening for at-risk adolescents in primary care settings: Diabetes screening adolescents with A1c. Pediatr Diabetes 2013; 14: 512–518. doi: 10.1111/pedi.12037
26. Kim MS, Jo DS, Lee DY. Comparison of HbA1c and OGTT for the diagnosis of type 2 diabetes in children at risk of diabetes. Pediatr Neonatol 2019; 60: 428–434. doi: 10.1016/j.pedneo.2018.11.002
27. Chan CL, Pyle L, Newnes L, et al. Continuous Glucose Monitoring and its Relationship to Hemoglobin A1c and Oral Glucose Tolerance Testing in Obese and Prediabetic Youth. J Clin Endocrinol Metab 2015; 100: 902–910. doi: 10.1210/jc.2014-3612
28. Bergman M, Abdul-Ghani M, DeFronzo RA, et al. Review of methods for detecting glycemic disorders. Diabetes Res Clin Pract 2020; 165: 108233. doi: 10.1016/j.diabres.2020.108233
29. Santaguida PL, Balion C, Hunt D, et al. Diagnosis, prognosis, and treatment of impaired glucose tolerance and impaired fasting glucose. Evid Rep Technol Assess Summ 2005; 128: 1–11.
30. Soliman A, DeSanctis V, Yassin M, et al. Continuous glucose monitoring system and new era of early diagnosis of diabetes in high risk groups. Indian J Endocrinol Metab 2014; 18: 274. doi: 10.4103/2230-8210.131130
31. Helminen O, Pokka T, Tossavainen P, et al. Continuous glucose monitoring and HbA1c in the evaluation of glucose metabolism in children at high risk for type 1 diabetes mellitus. Diabetes Res Clin Pract 2016; 120: 89–96. doi: 10.1016/j.diabres.2016.07.027
32. Acciaroli G, Sparacino G, Hakaste L, et al. Diabetes and Prediabetes Classification Using Glycemic Variability Indices From Continuous Glucose Monitoring Data. J Diabetes Sci Technol 2018; 12: 105–113. doi: 10.1177/1932296817710478
33. El Awwa A, Soliman A, Al-Ali M, et al. Continuous glucose monitoring, oral glucose tolerance, and insulin – glucose parameters in adolescents with simple obesity. Georgian Med News 2012; 210: 47–53.