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Prediabetic risk factors among children and adolescents with obesity

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***Abstract*---**Type 2 diabetes mellitus, previously considered an adult disease but currently being observed in children and adolescents all over the world due to parallel increase in obesity. It is crucial to check obese children and adolescents for prediabetes to avoid long-term diabetes problems. This study aimed to identify a risk factors for prediabetes in obese children and adolescents. Method: A prospective case-control study was conducted on children aged 6-18 years at Al-Faiha Specialized Diabetes, Endocrine, and Metabolism Center (FDEMC) in Basra (South Iraq). Results: A total of 155 children participated in the study; 60% were males. Prediabetes was present in 44.5% (n=69) participants. The proportion of prediabetes by FBS was 40%, OGTT was 16.8%, and HbA1c was 37.4%. A family history of T2DM, diastolic blood pressure, physical activity, and triglycerides were found to be significantly associated with prediabetes (P-value <0.05). In a multivariate logistic analysis of risk factors; a family history of T2DM (OR = 0.205; CI =0.094-0.446; p-value < 0.0001), physical activity (OR = 3.059; CI =1.532-6.109; p-value=0.002), high triglycerides (OR, 2.888; CI: 1.241-6.722; p-value=0.014), and hypertension (OR, 0.447; CI: 0.230-0.868; p-value=0.017) were positive or negative significantly associated with the occurrence of prediabetes. Conclusion: Although the history of feeding, family history of T2DM, high triglycerides, high DBP, and lack of physical activity were significantly related to the incidence of prediabetes

***Keywords*---**prediabetes, risk factors, obesity, children and adolescents, Iraq.

Introduction

Prediabetes is a broad term that covers a variety aspects of abnormal metabolism of glucose, such as impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) or increased hemoglobin A1C (HbA1c), or combinations between these parameters. Each of these disorders, either discovered in childhood or adolescence. This leads to an increased likelihood of acquiring type 2 diabetes and other cardiovascular problems in adulthood (Weiss et al., 2017). Prediabetes is a reversible condition of glucose irregularities that is often linked with obesity and other metabolic disorders (Lee et al., 2017). It is characterized by elevated blood glucose levels that are greater than usual but not high enough to cause diabetes (O Akintayo-Usman et al., 2021). There are three criteria used by American Diabetes Association (ADA) to diagnose prediabetes: a fasting blood glucose level from 100mg/dl to 125mg/dl, or a hemoglobin A1c value from 5.7 % to 6.4 %, and a 2-hour oral glucose tolerance test (OGTT) reading of between 140mg/dl and 199mg/dl (Care & Suppl, 2020).

Historically, T2DM was seen as a disease of late adulthood, but in the Last few years, a prediabetes and T2DM have become increasingly widespread among children and adolescents; this shift is due to the rising incidence of overweight and obesity (Almari et al., 2018b). Childhood obesity has become a global health problem (Artati et al., 2013), According to the World Health Organization (WHO) Childhood obesity is one of the most serious public health issues of the 20th century (Casapulla et al., 2017). Obesity at an early age is linked with increase the chance to type 2 diabetes and may be lead to a lower life expectancy (Morandi & Maffeis, 2014). The same factors that lead to increase the risk of type 2 diabetes also lead to increase the risk of prediabetes: obesity, a large waist, a high-fat diet (including red meat, processed meat, and sugar-sweetened beverages), physical inactivity, advanced age, race, family history, gestational diabetes(GD), polycystic ovary syndrome, obstructive sleep apnea, and tobacco use (Hsu et al., 2021). Diabetes and cardiovascular disease are more likely in those with prediabetes than in those who do not have it (Care & Suppl, 2019).

Methodology

This prospective case-control study was conducted at Al-Faiha Specialized-Diabetes-Endocrine and Metabolism Center (FDEMC) in Basra (South Iraq) over period from 1 November 2021 until the end of April 2022. 155 participants from obese children and adolescents aged from 6-18 years were included. All participants in this research were recorded for demographic characteristics and anthropometric measurements. They are measured for their height and weight on a calibrated scale without wearing shoes and heavy clothes. Both Height and weight are correct to 0.1 cm and 0.1 kg, respectively. BMI was measured from the ratio of the weight(kg) to the height squared(m2) and use the CDC Growth chart for to determine obesity (BMI ≥95th%) (Kuczmarski, 2002). Degree of obesity: obese ≥95th, Moderate Obesity ≥98th, Severe Obesity >99th

(Rappaport, 2007). Questionnaires were used to get information from a participant about family history of T2DM, steroid use, maternal history of gestational diabetes during child pregnancy, physical activity (according to WHO, at least 30min/d or 150 min/week), and their history of breast feeding.

Appropriate cuff size is used to measure blood pressure (BP). Before measuring BP, the participant was instructed to rest for at least 10 minutes in an air-conditioned environment. A calibrated sphygmomanometer was used to measure systolic and diastolic blood pressure in the supine position on the right arm, Hypertension (SBP and/or DBP in the ≥ 95th percentile) (Flynn & Falkner, 2017). The presence of acanthosis nigricans was determined by observing the neck fold by the physician. Also, Fasting lipid profiles (LDL, HDL, TG, and total cholesterol) were assessed for all participants in this study. According to the American Diabetes Association (ADA), the participant diagnosed as prediabetes if fasting blood sugar from 100mg/dl to 125mg/dl(fasting 8-10 hours), and/or 2-hour oral glucose tolerance ranging from 140mg/dl to 199mg/dl, in addition to HbA1c (5.7% -6.4%)(Care & Suppl, 2020). In OGTT, participants were given 1.75g of glucose orally per kg of body weight (max-75g) in 250 ml of water and they told to wait 2 hours without activity to test glucose level after 2 hours.

Statistical analysis

The data was collected through a questionnaire. The information for each question was transferred to code sheets. The statistical analysis was carried out using SPSS 25. The data was shown in simple frequency, percentage, mean, and standard deviation measures. The Chi-square test was applied to see if there was a significant difference for different percentages (qualitative data). Statistical significance was taken into account when the P-value was less than 0.05. Also, binary multivariate conditional logistic regression was used to analyze the risk factors for prediabetes.

Results

The basic demographic characteristics in the studied samples is summarized in Table 1. A total of 155 participants (69 with prediabetes and 86 with normal glucose level) aged 6 to 18 years, with a mean age of 11.60±3.27 years. The age (6-18 years) was subdivided into three groups, the first group was 6-9 years (children), the second group was 10-13 years (middle adolescents), and the third group was 14–18 (late adolescent) years. The maximum number 47.1% (n=73) of participants belonged to the 10–13 age group. Also, 60% (n=93) were males, while 40% (n=62) were females. The majority of participants 75.5% (n=117) were from urban areas, and 53.5% (n=83) had a medium socioeconomic status. A larger proportion 60.6% (n=94) of participants were in the primary stage, followed by 36.8% (n=57) in the secondary stage. However, there was no demographically significant difference between prediabetic and non-prediabetic participants (p-value>0.05).

Table 1
Basic socio-demographic characteristics of the studied sample

Variables		Study sample			P. value
		Prediabetes (n=69)	No prediabetes (n=86)	Total (n=155)	
Age groups	6-9 years	17 (24.6%)	20 (23.3%)	37 (23.9%)	0.277
	10-13 years	28 (40.6%)	45 (52.3%)	73 (47.1%)	
	14-18 years	24 (34.8%)	21 (24.4%)	45 (29%)	
	Mean± SD (Min-Max)		11.60±3.27 (6-18)		
Gender	Male	42 (60.9%)	51 (59.3%)	93 (60%)	0.843
	Female	27 (39.1%)	35 (40.7%)	62 (40%)	
Residence	Urban	52 (75.4%)	65 (75.6%)	117 (75.5%)	0.975
	Rural	17 (24.6%)	21 (24.4%)	38 (24.5%)	
Education	Primary	39 (56.5%)	55 (64.0%)	94 (60.6%)	0.642
	Secondary	28 (40.6%)	29 (33.7%)	57 (36.8%)	
	Illiterate	2 (2.9%)	2 (2.3%)	4 (2.6%)	
	Primary	16 (23.2%)	25 (29.1%)	41 (26.4%)	
	Secondary	18 (26.1%)	19 (22.1%)	37 (23.9)	
	University or high	18 (26.1%)	20 (23.3%)	38 (24.5%)	
Socioeconomic status	Low	29 (42.0%)	41 (47.7%)	70 (45.2%)	0.245
	Medium	38 (55.1%)	45 (52.3%)	83 (53.5%)	
	High	2 (2.9%)	0 (0.0%)	2 (1.3%)	

*Chi-squared test

Figure 1: shown the proportion of prediabetes by FBS, 2h-OGTT and HbA1c were FBS (40%), HbA1c (37.4%), and OGTT (16.8%). This proportion differed from one study to another, this difference might be related to the various screening methods or criteria utilized in these studies as well as the characteristics of the participants.

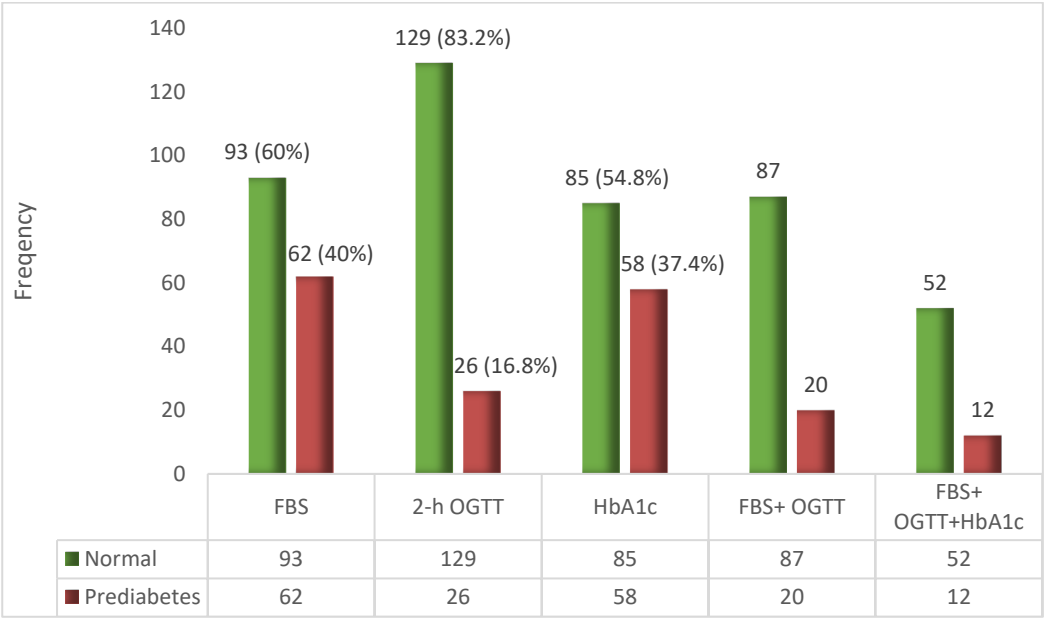

Figure 1. distribution of study sample by FBS, OGTT, and HbA1c (ADA criteria)

Table 2 showed that 52.3% (n=81) of participants were exclusively breastfed in the first six months of life. While, 25.8% (n=40) with formula feeding and 21.9% (n=34) were mixed between breast and formula feeding (p-value=0.01). Additionally, 66.7% (n=46) of participants who diagnosed as prediabetic had a family history of T2DM (first-degree relative). In comparison, 33.3% (n=23) did not have a family history of T2DM (p-value<0.001). Moreover, this study demonstrated that a large proportion 66.7% (n=46) of obese children and adolescents with prediabetes, have acanthosis nigricans (p-value=0.037). Also, a high percentage (75.4% (n=52) of participants with prediabetes lived a sedentary lifestyle (inactive), followed by 24.6% (n=17) of them who were active. 37(53.6 %) of the participants with prediabetes had a high LDL (p-value=0.058) and 47.8% (n=33) with low HDL. At the same time, 30.4% (n=21) from those with prediabetes were had high triglyceride (p-value=0.012). also, this study revealed that 30.4% (n=21) of prediabetic participants had high systolic blood pressure, and 31.9% (n=22) had high diastolic blood pressure. However, these results also found a significant relationship between prediabetes and steroid use (p-value=0.036).

Table 2
Distribution of the studied sample according to Medical history of participants

Variables		Study sample			P. value
		Prediabetes (n=69)	No Prediabetes (n= 86)	Total (n=155)	
History of feeding (first 6 months of life)	Exclusive breast feeding	30 (43.5%)	51 (59.3%)	81 (52.3%)	0.010*
	Formula feeding	26 (37.7%)	14 (16.3%)	40 (25.8%)	

	Mixed	13 (18.8%)	21 (24.4%)	34 (21.9%)	
Steroid drug	Yes	22 (31.9%)	15 (17.4%)	37 (23.9%)	0.036*
	No	47 (68.1%)	71 (82.6%)	118 (76.1%)	
Maternal history of GDM	Yes	17 (24.6%)	10 (11.6%)	27 (17.4%)	0.053
	No	52 (75.4%)	74 (86.0%)	126 (81.3%)	
	I do not know	0 (0%)	2 (2.4%)	2 (1.3%)	
Family history of T2DM	Yes	46 (66.7%)	29 (33.7%)	75 (48.4%)	<0.001 *
	No	23 (33.3%)	57 (66.3%)	80 (51.6%)	
Acanthosis nigricans	Yes	46 (66.7%)	43 (50.0%)	89 (57.4%)	0.037*
	No	23 (33.3%)	43 (50.0%)	66 (42.6%)	
LDL(mg/dl)	Normal	32 (46.4%)	53 (61.6%)	85 (54.8%)	0.058
	High	37 (53.6%)	33 (38.4%)	70 (45.2%)	
HDL(mg/dl)	Low	33 (47.8%)	30 (34.9%)	63 (40.6%)	0.223
	Normal	34 (49.3%)	51 (59.3%)	85 (54.8%)	
Total Cholesterol (mg/dl)	High	2 (2.9%)	5 (5.8%)	7 (4.5%)	0.238
	Normal	48 (69.6%)	67 (77.9%)	115 (74.2%)	
TG (mg/dl)	High	21 (30.4%)	19 (22.1%)	40 (25.8%)	0.012
	Normal	50 (72.5%)	76 (88.4%)	126 (81.3%)	
SBP (mmHg)	Yes	21 (30.4%)	18 (20.9%)	39 (25.2%)	0.175
	No	48 (69.6%)	68 (79.1%)	116 (74.8%)	
DBP (mmHg)	Yes	22 (31.9%)	12 (14.0%)	34 (21.9%)	0.007*
	No	47 (68.1%)	74 (86.0%)	121 (78.1%)	
Degree of obesity	Obese	8 (11.6%)	8 (9.3%)	16 (10.3%)	0.832
	Moderately obese	15 (21.7%)	17 (19.8%)	32 (20.6%)	
	Severely obese	46 (66.7%)	61 (70.9%)	107 (69.0%)	
Physical activity	Yes	17 (24.6%)	43 (50.0%)	60 (38.7)	0.001 *
	No	52 (75.4%)	43 (50.0%)	95 (61.3%)	

*Chi-squared test

All factors associated with prediabetes were included in the multivariable logistic regression analysis model in table 3.

Table 3
Multivariable logistical regression analyzed of risk factor for prediabetes

variables		B	Wald	Sig.	OR	(95% CI) Lower	Upper
Physical activity (at least 30 min/day)	Yes	Reference					
	No	1.118	10.035	0.002	3.059	1.532	6.109
	Constant	-0.928-	10.492	0.001	0.395		
History of breast feeding	Exclusive breast feeding	Reference					
	Mixed	1.028	4.908	0.027	2.794	1.126	6.936
	Formula	0.214	0.192	0.661	1.238	.476	3.218

	feeding						
Steroid drug	Yes	Reference					
	No	-.857-	3.149	.046	2.216	1.044	4.703
Maternal	Yes	Reference					
history of	No	-.762-	2.185	.139	.467	.170	1.282
GDM	I do not know	-20.259-	.000	.999	.000	.000	.
Family history	Yes	Reference					
of T2DM	No	-1.585-	15.951	.000	.205	.094	.446
Hypertension	Yes	Reference					
(mmHg)	No	-0.805-	5.661	0.017	0.447	0.230	0.868
	Constant	0.278	1.096	0.295	1.320		
Acanthosis	Yes	Reference					
nigricans	No	-0.693-	4.300	0.038	0.500	0.260	0.963
	Constant	0.067	0.101	0.751	1.070		
TC(mg/dl)	Normal	Reference					
	High	0.434	1.382	0.240	1.543	0.749	3.178
	Constant	-0.333-	3.110	0.078	0.716		
LDL(mg/dl)	Normal	Reference					
	High	0.619	3.566	0.059	1.857	0.977	3.530
	Constant	-0.505-	5.080	0.024	0.604		
HDL(mg/dl)	Low	Reference					
	Normal	-0.501-	2.226	0.136	0.606	0.314	1.170
	High	-1.012-	1.340	0.247	0.364	0.066	2.016
	Constant	0.095	0.143	0.706	1.100		
TG (mg/dl)	Normal	Reference					
	High	1.061	6.054	0.014	2.888	1.241	6.722

Discussion

Our study indicated that 60.9 % (n=42) of participants with prediabetes were male. However, there was no statistically significant link between gender and prediabetes (p-value= 0.843). These results agreed with a study in South India (Krishnappa et al., 2017). In general, there was no statistically difference in demographical characteristics between prediabetic and non-prediabetic participants (p-value<0.05). This study found that the history of feeding (first six months of life) was significantly associated with prediabetes (p-value = 0.01). This finding confirms a prior study by (Nadeau & Dabelea, 2008), which revealed that breastfeeding protects against the development of T2DM in later life. Additionally, this study found that participants who had taken steroid medications were a significant risk factor for prediabetes (p-value = 0.036). Glucocorticoids lead to hyperglycemia via insulin resistance, increasing hepatic gluconeogenesis and decreasing peripheral tissues' glucose uptake (Kim et al., 2011).

Physical activity and a Family history of T2DM were a highly significant risk factor for prediabetes. Our results were Similar with the findings of a study by (Wang et al., 2018), which was conducted on children and adolescents aged 6–17 years in China. Also, our results showed that DBP was significantly correlated with prediabetes (p-value =0.007). At the same time, SBP was not significantly correlated with prediabetes (p-value =0.175). This result consistent with a study

by (Krishnappa et al., 2017). In addition, these results showed a significant correlation between prediabetes and triglyceride (TG) (p. value =0.012), while no significant correlations were observed with regard to (LDL, HDL, and cholesterol) (P. value >0.05). This result confirmed the finding of a study conducted on obese children and adolescents in Europe (Kleber et al., 2010).

This study did not find any statistical association between prediabetes and the maternal history of GDM. our result different with a cross-sectional study among adolescents in Kuwait (Almari et al., 2018a) , which found a significant correlation between prediabetes and maternal diabetes. This difference in the results may be due to the application of a healthy diet pattern by children who are born to diabetic mothers, or because they have high physical activity. In Multivariate logistic analysis of risk factors for prediabetes among the studied samples, The present study found that participants without hypertension had 0.447 times lower than those with hypertension to develop prediabetes (OR, 0.447; CI: 0.230-0.868; p-value=0.017). This study consists with the study done by (Wallace et al., 2020). Triglyceride remains the only lipid profile variable associated with prescience prediabetes, the probability of getting prediabetes was significantly higher 2.888 times among high triglyceride participants than normal triglyceride(OR, 2.888; CI: 1.241-6.722; p-value=0.014). These results confirm the results of a study by (Al Amiri et al., 2015), which used univariate logistic regression(OR=2.28; CI: 1.11–4.68; p-value 0.024).

The current study, revealed that obese children and adolescents who had Inadequate physical activity were had 3.059 times more likely to have prediabetes (OR = 3.059; CI =1.532-6.109; p-value=0.002) compared with those had adequate physical activity. This finding consistent with a cross-sectional study in New Zealand by (Mazahery et al., 2021). Participants who had never used steroids medication had a 2.216 times lower risk of developing prediabetes compared with those who had used steroids medication (OR=2.216; CI=1.044-4.703; p-value=0.046). The risk of developing steroid-induced diabetes rises in direct proportion to the amount of the medicine used and the length of time it is taken. Furthermore, the current study found that the risk of developing prediabetes was 0.205 times lower in those with no family history of T2DM than in those with a family history of T2DM (OR = 0.205; CI =0.094-0.446; p-value < 0.0001). This result agreed with a descriptive cross-sectional study by (Martins et al., 2017), which discovered that participants with a positive family history of diabetes had 1.57 times higher probability to get prediabetes than those who did not have a positive family history of diabetes (OR = 1.57; 95 CI= 1.088–2.611; p-value=0.023).

Conclusion and Recommendation

In our study, low physical activity, high triglyceride, high diastolic blood pressure, family history of T2DM were identified as risk factors for prediabetes. American Diabetes Association advises screening children with risk factors for T2DM, Iraqis obese children should be examined at a younger age. As well as lifestyle modifications such as weight reduction, good eating habits, and adequate physical activity, may help to prevent the onset of T2DM. Follow up studies are

needed to investigate which of the approaches is more accurate in predicting prediabetes.

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