Cardio-Metabolic Risk Factors in Iranian Children: Where We are and the Others?

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Abstract- Rising obesity incidence and its complications have lead to change of our view about cardio-metabolic risk factors and need of reassessment of these complications in childhood age. The aim of current study was to evaluate prevalence of obesity and related cardio-metabolic risk factors of children. This was a cross-sectional study in a representative sample of 12 years old children in Rasht, the biggest city in north of Iran. Participants were interviewed and examined by a trained research team and demographic characteristics, detailed examination (height - weight - blood pressure) were recorded. Blood samples were drawn for biochemical testing including Fasting blood sugar, Triglyceride, Cholesterol, HDL & LDL. Data analysis was done using SPSS software. Total participants were 858 children and 550(64%) were male. Prevalence of underweight, normal weight, overweight, obese were 22.5%, 54.4%, 11.3%, 11.8%, respectively. The prevalence of cardio-metabolic risk factors included hypercholesterolemia (6.7%), hypertriglyceridemia (33.6%), high LDL (5.9%), low HDL (28 %), high systolic (7.6%) & diastolic blood pressure (10.6%) (>90th percentile) and abnormal carbohydrate metabolism (12%) revealed hypertriglyceridemia as the most common dyslipidemia. Correlation analysis didn't show significant correlation between BMI & FBS but LDL, Cholesterol and TG had week positive correlation with BMI (Pearson correlation: 0.161, 0.285, 0.222 respectively, p value <0.001). Obesity and dyslipidemia are common problems in this area and we should note to screen cardiometabolic risk factors in addition of obesity, especially in children with rapid weight gain. This study highly recommended more investigation to evaluate final effect of these factors in adulthood.

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Introduction

Childhood obesity has increased dramatically (1,2). Epidemy of childhood obesity in the United States has been accompanied by an increase in the prevalence of pre diabetes and type 2 diabetes (T2DM) among children and adolescents (3).

Youth with metabolic syndrome (Mets) are at increased risk in adulthood, however, the simplicity of screening for high BMI or overweight and obesity in the pediatric setting offers a simpler, equally accurate alternative to identifying youth at risk of developing adult Mets, or T2DM, Magnussen et al report (4,5). Obesity and overweight have become a problem of public health that is associated with substantial economic burden in both developed and developing countries.

The number of overweight children and adolescents

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were doubled in the last two decades in the United States and worldwide, including developing countries (6). Obesity in children affects their health in both short and long-term.

Although the obesity and its preventive strategies are poorly understood but increasing number of these children and adolescents requires a substantial investigation of primary and secondary preventive strategies in addition of novel approaches in the treatment modalities (6).

Complications of childhood obesity continues to adulthood as cardiovascular disease risk factors; especially hypertension in adulthood has a considerable correlation with childhood obesity and blood pressure (BP) level, as one of best predictor of hypertension in adulthood (7-9).

Despite increasing knowledge about risk factors of cardiovascular diseases, prevalence of obesity among children and adolescents is increasing. In America, childhood obesity has increased dramatically over the past three decades. Data from the third national health and nutrition survey in the U.S. conducted between 1998-1991 showed that the prevalence of obesity in children and adolescents aged 6- 17 based on the 95th and 85th percentiles of BMI is 10.9% and 22% respectively (10).

In addition of increasing prevalence of obesity in the world, limited information were available about developing countries (11). Minimal clinical manifestation of these problems and significant cardiovascular complications mandate screening in high risk population, such as obese children, to prevent cardiovascular and metabolic complications in adulthood.

Materials and Methods

Participants were selected from 12 years old girls and boys' students from different area of Rasht city. All of these participants were examined by physician of health centers and data were recorded. Total numbers of participants were 2305 students in junior level who had referred for physical examinations to the 15 urban health centers in Rasht.

After classified proportionate to size in different regions of Rasht, the first case in each health center was randomly assigned and then with consideration of interval, the next case was examined. If the parent of the student was not satisfied, the next participant was recruited in the study.

Before starting the study, all of colleagues including physicians, supervisor and executive coordinators met each other for required coordination and guide to complete research questionnaire.

The questionnaires included demographic information, history of any disease in students and their first and second degree relatives, clinical examination (measuring height, weight, blood pressure, body mass index and physical examination of various organs).

Clinical examination tools' were similar in all centers and calibrated to enhance validity and reliability of measurements.

Also the validity and reliability of that inventory had been investigated by five physicians.

Consent letters were obtained from students and their parents and then all participants were referred to the referral lab in Rasht for laboratory tests including FBS, BS, and Cholesterol. TG, LDL, HDL and insulin level (if necessary).

These labs had quality accreditation of laboratory department of ministry of health. Results of these tests were registered in the questionnaire.

Data analysis was done by SPSS software, version 14. The main statistical tests were Pearson correlation analysis, paired T test, and ANOVA test.

Results

A total of 858 adolescent were recruited in the study including 550 (64%) boys. Table 1 presents sex distribution, body size measurements, mean of blood pressure and biochemistry laboratory data as FBS, LDL, HDL, TG, Cholesterol, categorized based on BMI in four categories.

Prevalence of overweight and obesity were 31.5 %(15% + 16.5 %), in summation, without significant difference between male and female partcipants. Different percentiles of boys and girls and lipid profile are summarized in table 2.

To find high risk populations and compare with other studies, table 3 categorizes prevalence of cardio-metabolic risk factors based on BMI. Abnormal cutoff for blood pressure and laboratory results have been determined based on standard reference tables (12).

Table 3 presents significant difference between prevalence of cardio-metabolic risk factors with rising of BMI.

Correlation analysis was shown in table 4 that indicates all investigated risk factors related to BMI except FBS.

Table 1. Demographic characteristics and mean of glucose and lipid profile measurements

		BMI					
		Underweight (BMI < 5)	Normal (5<BMI ≤85)	Overweight (85<BMI≤95)	Obesity (BMI > 95)	Total	*P*.value
Sex	**Male n. (%)**	72(14.6)	262(53.1)	77(15.6)	82(16.6)	493(100)	P value >0.05 c
	Female n. (%)	28(10.8)	153(59.1)	36(13.9)	42(16.2)	259(100)	
	Total n. (%)	100(13.3)	415(55.2)	113(15)	124(16.5)	752(100)	
Waist circumference	**Mean (+/-SD)**	59.9(8.3)	66.1(7)	77.6(5.9)	87.9(12.1)	70.8(12.2)	P value <0.001 a
Hip circumference	**Mean (+/-SD)**	75.4(7.2)	80.8(6.3)	91(6.6)	98(11.1)	84.7(10.7)	P value <0.001 b
Systolic blood pressure	**Mean (+/-SD)**	92.5(10.5)	96(10.1)	99.7(10.6)	105.9(14.6)	97.8(11.8)	P value <0.001 h
Diastolic blood pressure	**Mean (+/-SD)**	60.3(7.3)	61.8(7.9)	62.4(8.6)	66.8(9.4)	62.5(8.4)	P value <0.001 m
FBS	**Mean (+/-SD)**	92.2 (7.2)	92.7(6.8)	92.8(8.1)	93.4(7)	92.8(7)	P value >0.05 c
Total cholesterol	**Mean (+/-SD)**	149.5(23.8)	152.3(27.9)	168.7(38.7)	165.2(27.3)	156.5(30)	P value <0.001d
Triglyceride	**Mean (+/-SD)**	74.1(33.2)	97.3(59.5)	129.4(77.7)	145.8(76.7)	107(67)	P value <0.001e
HDL	**Mean (+/-SD)**	45.8(8.8)	44.0(9)	42(8.6)	40.3(9.1)	43.3(9)	P value <0.001f
LDL	**Mean (+/-SD)**	88.9(20.9)	89.9(22)	102.2(29.6)	96.0(23.3)	92.6(23.8)	P value <0.001g

a: Obese children had significant larger waist circumference than other groups (*P* <0.001), **b**:Obese children had significant larger hip circumference than other groups (*P*<0.001), **c**:No significant difference was between groups, **d**:Obese and overweight groups had significant higher total cholesterol than underweight and normal group (*P* <0.001), **e**:Obese and overweight groups have significant higher Triglyceride than Underweight and normal group (*P* <0.001), **f**:Obese have significant lower HDL than underweight and normal group (*P* <0.001) and overweight group had significant lower HDL than underweight and normal group (*P* <0.001), **g**:overweight group had significant higher LDL than underweight and normal group (*P* <0.001), **h**:Systolic blood pressure had an crescendo pattern with significant change between four groups; Underweight < Normal < Overweight < Obese, **m**:Diastolic blood pressure had an crescendo pattern with significant change between four groups; Underweight < Normal < Overweight < Obese
SD: Standard deviation, n. : number

Table 2. Lipid profile percentiles of boys and girls

Test		**Total cholesterol (mg/dl)**		**TG (mg/dl)**		**HDL (mg/dl)**		**LDL(mg/dl)**	
Sex		**Boys**	**Girls**	**Boys**	**Girls**	**Boys**	**Girls**	**Boys**	**Girls**
Number	**Valid**	547	308	549	309	549	309	549	309
Mean		158.20	155.56	105.03	113.18	43.99	41.88	93.54	91.06
Std. Deviation		29.29	26.99	65.48	72.51	9.34	8.648	24.71	22.36
Percentiles	**5**	119.0	115.45	39.0	41.5	31.0	29.0	58.0	58.0
	50	155.0	153.0	84.0	97.0	43.0	41.0	92.0	91.0
	75	173.0	172.0	133.0	132.0	49.0	47.0	107.0	104.0
	95	212.6	208.55	228.5	240.5	62.0	57.5	136.0	131.0

Discussion

Life style change impacts all aspects of health. The major impact of these changes is on obesity and related complications. Now, with multiple reports of rising incidence of obesity and our knowledge about its cardio-metabolic complications, accurate determination of obesity prevalence and its complications is warranted to plan for long-term strategies (1,13-16).

Interestingly prevalence of cardio-metabolic risk factors was same as other reports from different ethnicities and environments. We have 12% High FBS, 28% low HDL, 5.9% high LDL, 6.7% hypercholesterolemia and 33.6% hypertriglyceridemia that was the most common dyslipidemia.

Reference data of national institutes of health in 1980 also has the same distribution for dyslipidemia as 12.3%, 28.7%, 4%, 6.2% and 34.1% for abnormal carbohydrate metabolism, low HDL, high LDL hypercholesterolemia and hypertriglyceridemia, respectively (12).

In 2008 Fesharakinia and colleagues reported different prevalence of dyslipidemia in aged matched group of Iranian population. They report low HDL as the most common dyslipidemia with 14.1 % prevalence and 4.1%, 3% and 5.4% for high LDL, hyper cholesterolemia and hypertriglyceridemia, respectively (17). Other epidemiologic studies didn't reveal the same results and most of them reported hypertriglyceridemia as the most prevalent disorder and the others in a relatively same range of current study, especially when they focused on obese children (18-21). Some of them indicated hypercholesterolemia as the most prevalent dyslipidemia (22). It seems we have no significant changes in dyslipidemia pattern and prevalence in comparison to recent studies.

Table 3. Prevalence of cardio-metabolic abnormalities

			BMI Categorized				
			Underweight (BMI < 5)	**Normal (5< BMI ≤85)**	**Overweight (85<BMI≤95)**	**Obesity (BMI > 95)**	**Total**
Systolic blood pressure >95th percentile	**No**	**Count**	95	398	105	109	707
		Percent[a]	99.0%	99.7%	97.2%	88.6%	97.4%
	Yes	**Count**	1	1	3	14	19
		Percent[a]	1.0%	0.3%	2.8%	**11.4%**	2.6%
Systolic blood pressure >90th percentile	**No**	**Count**	94	389	97	91	671
		Percent[a]	97.9%	97.5%	89.8%	74.0%	92.4%
	Yes	**Count**	2	10	11	32	55
		Percent[a]	2.1%	2.5%	10.2%	**26.0%**	7.6%
Diastolic blood pressure >95th percentile	**No**	**Count**	88	350	91	94	623
		Percent[a]	96.7%	91.4%	88.3%	78.3%	89.4%
	Yes	**Count**	3	33	12	26	74
		Percent[a]	3.3%	8.6%	11.7%	**21.7%**	10.6%
Diastolic blood pressure >90th percentile	**No**	**Count**	88	350	91	94	623
		Percent[a]	96.7%	91.4%	88.3%	78.3%	89.4%
	Yes	**Count**	3	33	12	26	74
		Percent[a]	3.3%	8.6%	11.7%	**21.7%**	10.6%
HDL > 40	**No**	**Count**	19	96	40	55	210
		Percent[a]	19.0%	23.2%	35.4%	44.4%	28.0%
	Yes	**Count**	81	318	73	69	541
		Percent[a]	81.0%	76.8%	64.6%	**55.6%**	72.0%
FBS categorized	**Less than 100**	**Count**	88	369	96	108	661
		Percent[a]	88.0%	89.1%	85.0%	87.1%	88.0%
	More than 100	**Count**	12	45	17	16	90
		Percent[a]	12.0%	10.9%	15.0%	12.9%	12.0%
LDL >95th percentile	**No**	**Count**	96	397	100	114	707
		Percent[a]	96%	95.9%	88.5%	91.9%	94.1%
	Yes	**Count**	4	17	13	10	44
		Percent[a]	4%	4.1%	**11.5%**	8.1%	5.9%
Cholesterol >95th percentile	**No**	**Count**	97	395	96	113	701
		Percent[a]	97	95.4%	85%	91.1%	93%
	Yes	**Count**	3	19	17	11	50
		Percent[a]	3%	4.6%	**15%**	8.9%	6.7%
Triglyceride >95th percentile	**No**	**Count**	90	297	63	49	499
		Percent[a]	90%	71.7%	55.8%	39.5%	66.4%
	Yes	**Count**	10	117	50	75	252
		Percent[a]	10%	28.3%	**44.2%**	**60.5%**	33.6%

a: Percent in each BMI category

Bold and underlined: cell show significant statistical difference rather than other related cells (*P*.value <0.01)

Table 5. Correlation analysis

	Analysis	Weight	SBP	DBP	BW	FBS	Cholesterol	Triglyceride	HDL	LDL	Insulin level
BMI	**Pearson correlation**	0.808	0.314	0.217	0.137	0.016	0.222	0.285	-0.128	0.161	0.556
	***P*.value**	0.000	0.000	0.000	0.001	N/S*	0.000	0.000	0.000	0.000	0.000
	Number	752	726	697	546	751	748	751	751	751	90

N/S*: not significant

SBP: Systolic Blood pressure, DBP: Diastolic Blood pressure, BW: Birth weight

In comparison to other age matched studies, prevalence of childhood obesity is same as other reports from developed and developing countries (1, 14, 23, 24). It has crescendo pattern in comparison to previous studies from Iran, 16.5% in this study versus 12.3%, 12%, 7.1% that was reported by Hajian et al, Behzadnia et al and Moayeri et al respectively; But prevalence of overweight doesn't follow this rule, 15% versus 12.3%, 27.4% and 17.9% respectively for previously mentioned studies(16, 25, 26). Crescendo pattern also reported by different studies but with plateau pattern in recent years (27). Olds et al indicated high rate of obesity in different areas that was stabilized in recent years after a rapid increase. Hypothesis regardoffing this data is related to different factors such as sex, ethnicity, socioeconomic state, etc, and need more detailed studies. Regardless of this pattern high rate of obesity highlights need of more investigation about risk factors and complication of obesity.

Obese Children have more abnormal lipid profile including Low HDL (40.3 ± 9.1 v/s 44.0 ± 9) and High LDL (96.0 ± 23.3 vs 89.9 ± 22), cholesterol (165.2 ± 27.3 vs 152.3 ± 27.9) and triglyceride (145.8 ± 76.7 vs 97.3 ± 59.5) than normal weight children. They also presented with higher blood pressure rather than normal Childs. Different aspects of these results are investigated by multiple authors and same results are reported in blood pressure changes (28), and lipid profiles (4, 14, 29), but the exact effect of these finding on final outcome in adulthood are not clear. Li s et al in a five years study (the Bogalusa Heart Study) show "the MHO (metabolically healthy overweight/obesity) phenotype starts in childhood and continues into adulthood" with comparable lipid profile to non overweight/obese adult (15). But they also report positive correlation of Carotid artery intima-media thickness (IMT) as related cardiovascular risk factor with high LDL-cholesterol level (15). These findings clearly show obese children are more susceptible to cardiovascular complications due to higher rate of abnormal lipid profile and highlighted lipid profile analysis to categorized obese children to MHO and non-MHO group.

Correlation analysis of these risk factors show significant positive but not a linear correlation between BMI and LDL, Cholesterol and TG (Pearson correlation: 0.161, 0.285, 0.222 respectively with p value <0.001). Interestingly FBS was not correlated to BMI and the mean of FBS has no significant difference between four BMI categories. On the other hand, Insulin level shows the most significant and linear correlation with BMI (+0.55), indicating the effect of obesity on insulin resistance. It should be reemphasized that we check insulin level in patients with impaired fasting glucose. Correlation of BMI and insulin level and simultaneously no correlation with FBS, reported by multiple investigations (30-32). In fact obesity is an independent risk factor for insulin resistance but association to childhood diabetes mellitus needs more investigation. Clear impact of high BMI on insulin resistance, not on diabetes mellitus, needs more accurate interpretation of BMI as a screening tool for diabetes mellitus patients. Pattern of BMI changes is the more sensitive and specific indicator in diabetes mellitus screening rather than a net BMI measurement. Sinha et al report high rate of impaired glucose tolerance test, 25%, secondary to insulin resistance among obese children (3). So in obese patients using impaired glucose tolerances test rather than FBS or notice to pattern of BMI change (to find rapid weight gain) is more sensitive clue to find insulin resistance. To find exact relation of this abnormal carbohydrate metabolism and development of diabetes mellitus conducting more cohort studies are warranted.

Relatively high prevalence of obesity and correlation of it to cardio-metabolic risk factors and also high rate of dyslipidemia among Iranian children indicate planning to screen these risk factors in children, especially children with rapid weight gain. It is also recommended to conduct more studies to evaluate final effect of these factors in adulthood.

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