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Children's Health is Insulin and Lipid Dependent

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Abstract: To assess the differences in fasting blood glucose, insulin and lipids of children having family history of diabetes or heart disease in first or second degree relative compared with a control group. Questionnaire was given to collect demographic data and to assess the dietary habits and family history of these children. Demographic data, anthropometric measurements and blood samples for fasting blood glucose, insulin and lipids of children from 4 schools was taken. The samples of ninety nine children were collected and sent to Baqai Institute of Diabetology and Endocrinology, Karachi to assess their biochemical parameters. Children having positive family history for diabetes had slightly mean values for BMI as compared to the controls but the differences were not statistically significant. Overweight risk children (>85th Percentile of BMI for age) did not differ significantly in terms of various risk indicators however those who had a positive family history of diabetes had significantly higher percentage of abnormal Total Cholesterol, LDL-C, Insulin and low HDL. Diabetes and CVD risks in children having positive family history are probably mediated through increased weight. Thus information about family history augmented by body mass index could be used as an important screening tool for determining the risk status of children.

Key words: Insulin, blood glucose, diabetes, dietary habits

Introduction

Heart disease and diabetes are found to be highly prevalent in urban areas of Pakistan (Dodani *et al*., 1999). Currently Pakistan is 7th in the world according to WHO estimates with 7 million people with diabetes and it is expected to be 4th in the world with 15 million people with diabetes by the year 2025, representing a 2 fold increase (WHO, 1998; Diabetes Atlas, 2003).

Family history has shown a positive association with the incidence of diabetes (Shera *et al*., 1999) and heart disease among adults (Williams *et al*., 2001). The Bogalusa Heart Study has showed that even 5 to 10-year-old children have cardiovascular risk factors such as hyperlipidemia or elevated insulin levels and these risk factors increase substantially the risk of earlier cardiovascular disease in these individuals if they were tracked into adulthood (Srinivasan *et al*., 1996). It has been known for several decades now that hyper-cholesterolemia could be identified at an early age and intervention helps in reduction of risk of developing heart disease in later life (Szamosi *et al*., 1999).

More recently with the emergence of type 2 diabetes in children, screening of children for high insulin levels has also been suggested (Fagot *et al*., 2000; Cockram, 2000). Thus the need for additional information on the ability of detect adverse risk factors has been emphasized by the publication of guidelines that define overweight and hypercholesterolemia among children and adolescents (Whitaker *et al*., 1997; Himes and Dietz, 1994; NCEP, 1991).

By using recommended cut points, the current study examines the abnormal levels of lipids and insulin among 8-to 10 years-old.

In Pakistan it would also be justified to focus on high risk groups like children having family history of diabetes or heart disease as they are found to have higher than average risk for the development of these disorders (Hydrie *et al*., 2004).

Objectives:

1. To assess the biochemical parameters such as insulin and lipid levels in children with family history of Diabetes and Coronary Heart Disease compared with controls.
2. Data from diet and activity questionnaires was used to compare food consumption and activity pattern of children with family history of Diabetes and Coronary Heart Disease compared to controls.

Materials and Methods

Design: This was a cross sectional comparative study of three groups of children having family history of heart disease without diabetes, family history of diabetes with or without heart disease, No family history of diabetes or heart disease used as controls.

Subjects: Data was collected from school children in Karachi from October 2001 to May 2002. After getting informed consent from the parents, it was decided to recruit 132 children from four primary schools in Karachi,

Pakistan.

Three hundred and thirty three 8-10 year old school children agreed to take part in the study. In the first phase of the selection, all the children of corresponding age were screened for birth-weight, physical health history, family history of relevant diseases and current body weight status. According to the family history, children needed in each group were selected and the study explained to them and their parents. Finally all the eligible children were invited to participate in the second phase of the study. If the children and their parents were willing then letters for consent for participation in the study was taken from parents.

Out of 333 children who took part in this study 158 children were selected on the basis of family history. Out of these 63% (n=99) agreed to have the blood tests necessary for this study.

Data collection

Anthropometric measurements: Anthropometric measurements (height, weight, waist and hip) and blood samples were taken in school by a team of medical health professionals from Baqai Institute of Diabetology and Endocrinology.

Height was measured with a portable stadiometer following standard procedures (WHO, 1995). Portable weighing scale was used. All the subjects were weighed without shoes, in single layer of indoor clothing (WHO, 1995). Waist circumference measured by holding the non-stretchable measuring tape snugly around the waist at the midpoint between the bottom rib and tip of hipbone. Hip circumference was measured at the fullest part of the hips.

Blood test: Blood sample was collected by the laboratory staff of Baqai Institute of Diabetology and Endocrinology (BIDE) in schools and transported to lab for analysis within 30 minutes in appropriate containers (Sodium fluoride tubes for Glucose while other sample in plain test tube for serum analysis). Prior to testing blood, the fasting status confirmation sheet, signed by parents was received and subjects were also asked whether they had eaten or drank anything that morning. A doctor and a school teacher were present during the entire proceedings. Dieticians of BIDE ensured that breakfast was provided to all the children who came fasting. Blood was analyzed for fasting blood glucose, fasting insulin levels, total lipids, cholesterol, tri-glycerides, LDL & HDL.

Laboratory Determinations: High levels of Total Cholesterol and LDL-C were defined as those >200 mg/dl and >130 mg/dl, respectively while a triglycerides (T.G.) level $\geq$130 mg/dl was considered high, and an HDL-C level <35 mg/dl was considered low (Himes and Dietz, 1994; NCEP, 1991; AAP, 1998). Fasting Blood Sugars more than 125 was taken as abnormal while Insulin levels more than 8umol/dl was considered high.

Diet and activity: All the participating children filled a questionnaire about their usual diet and activity pattern. Data from diet and activity questionnaires was used to compare food consumption and activity pattern of children.

Data entry and analysis: Data entered and analyzed on SPSS version 10. Mean values of anthropometric measurements, diet and physical activity levels and biochemical parameters such as lipid profile and insulin levels in all the three groups was seen. The percentages of biochemical cut points levels in all three groups were also calculated. Significance of difference in categorical variables was assessed using chi-square test.

Results

The study was planned to have 44 children in each of the three groups i.e: those having family history of diabetes; those having family history of heart disease but not diabetes and controls with no family history for diabetes or heart disease. However due to difficulty in finding children having positive family history for heart disease but without diabetes only 14 children could be recruited in this group. In the other groups also parental reluctance to allow blood samples of their children to be drawn was a hindrance. Thus the resulting sample consisted of 44 children with family history of diabetes, 39 controls and 14 with family history of heart disease without diabetes. The children from the three groups did not had any statistically significant difference in mean age and birth weight as shown in Table 1.

Mean values for total cholesterol, triglycerides, HDL-C and LDL-C are given in Table 2. Mean values were significantly lower for HDL and higher for LDL in the group having family history of diabetes as compared to other groups. Children from the control group had significantly higher mean value for triglycerides.

Mean values for fasting blood sugars and fasting insulin are given in Table 3. Mean values for Fasting Plasma Glucose were significantly higher among those having family history for Cardio-vascular disease. Mean insulin value was also markedly higher among this group but the difference did not reach statistical significance.

Percentages of above normal insulin and lipid profile levels in all three groups are shown in Fig. 1.

Mean values for Body Mass Index and waist-hip ratio are given in Table 4 . Difference between the three groups reached statistical significance only for Body Mass Index with the group with family history for diabetes had the highest mean values for BMI.

Physical activity habits and food habits of children were also compared. Children having family history for

Table 1: Age sex and birth weight of children

		Family History					
		Control		Diabetes		CVD	
		Male	Female	Male	Female	Male	Female
	n	17	18	19	24	6	8
AGE (years)	Mean	9.94	9.50	9.56	9.70	9.67	9.50
	SD	0.85	0.86	0.51	0.70	0.82	0.53
Birth Weight (pounds)	Mean	6.96	7.38	7.05	6.97	7.30	6.46
	SD	1.66	1.27	1.13	1.24	0.67	1.46

Table 2: Mean values for indicators of dyslipedemia according to family history

	Control	Diabetes	CVD
	Mean ± SD	Mean ± SD	Mean ± SD
T. Lipids	630.8±52.1	608.9±68.3	612.6±51.2
T. Cholesterol	167.1±15.7	170.7±20.5	166.2±14.2
Triglycerides*P (0.001)	95.8±22.3	82.9 ±18.2	89.5±18.0
HDL* n-d (P = 0.043)	44.1±5.7	42.1±5.4	43.9±4.8
LDL* n-d (P = 0.019)	103.8±18.1	111.7±19.0	104.1±15.5

Table 3: Mean values for indicators of glycemic control according to family history

	Control	Diabetes	CVD
	Mean ± SD	Mean ± SD	Mean ± SD
Fasting Blood Sugar* d-h (p=0.031)	69.0±8.9	67.4±8.5	72.0±7.7
Insulin	6.1±2.7	6.0±3.7	6.5±2.7

Table 4: Mean values for BMI and WHR according to family history

	Control	Diabetes	CVD
	Mean ± SD	Mean ± SD	Mean ± SD
BMI* d-c, h P	15.2±2.3	16.1±3.2	14.3±2.0
WHR	0.9±0.0	0.8±0.1	0.8±0.1

Table 5: Mean values for indicators of physical activity level according to family history

	Control	Diabetes	CVD
	Mean ± SD	Mean ± SD	Mean ± SD
Weekly Reading Hours	14.8±6.8	14.8±8.2	17.1±8.6
Weekly Watching Hours	12.6±6.5	15.8±12.3	11.2±7.5
Weekly Running Hours	8.6±4.4	7.2±4.7	6.6±4.4

Table 6: Food habits (mean frequency per week) according to family history

	Control	Diabetes	CVD
	Mean ± SD	Mean ± SD	Mean ± SD
Fruit & Vegetables	11.3±2.5	10.9±2.0	11.3±1.6
Meat & egg*	8.9±1.4	9.7±1.4	9.1±1.6
Bread & Cereal*	12.9±1.6	13.0±1.7	14.6±1.3
Fried Food	2.9±0.7	2.8±0.7	2.6±0.9
Milk & its products	3.3±0.9	3.4±0.9	3.9±0.5
Sweet food	3.1±0.8	3.3±0.7	2.9±0.6

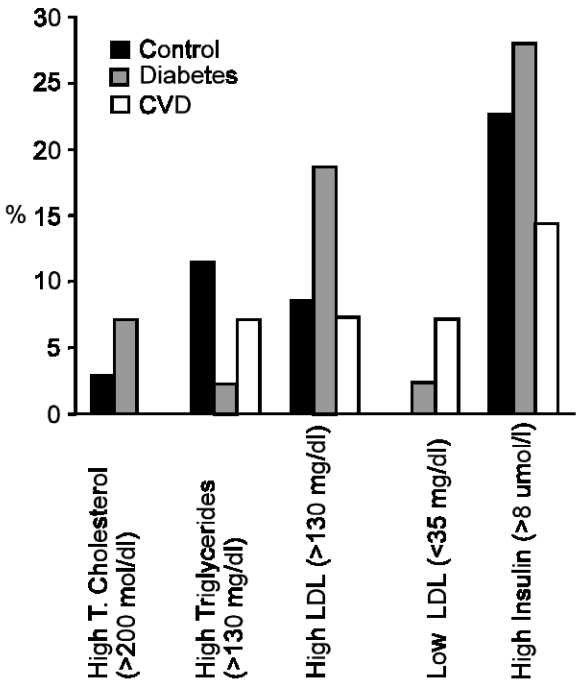

Fig. 1: Percentages of above normal insulin and lipid profile levels in all three groups

diabetes and heart disease on average spent more time in sedentary activities and less in running games as compared to controls; but none of these difference reached statistical significance (Table 5). Children with family history of diabetes ate meat and egg more frequently and those with family history of CVD ate bread and cereals more frequently ($P<0.01$ in each case) as compared to the controls (Table 6).

Discussion

Although family history has been found to be a strong predictor of CVD and diabetes risk in children, observations vary with age, sex and environmental factors (Burke *et al.*, 1991; Hulley and Newman, 1992; Davidson *et al.*, 1991; Starc *et al.*, 1991; Grech *et al.*, 1992; Castro *et al.*, 1993; Shea *et al.*, 1990). When the guidelines of the National Cholesterol Education Program were used to evaluate risk status, 91% of the subjects with very elevated cholesterol at follow-up could have been identified during childhood through cholesterol or obesity measurements (NCEP, 1991). In addition, an autopsy study of young adults who were killed accidentally was among the first to show that the progression of atherosclerotic plaques and cardiovascular risk had already begun in young adulthood (Mahoney *et al.*, 1996).

In the mid 1990s, several studies began to appear that showed the existence of visceral fat in children as early in life as age 6-7 y and showing significant correlation with risk factors such as fasting insulin and lipid concentrations. These relations were apparent across the spectrum of lean and obese individuals (Must *et al.*, 1992; Tershakovec *et al.*, 1998).

Because of the large increase in fibrous plaques in the coronary arteries of children and young adults who have 3 or 4CVD risk factors, the use of overweight as a screening tool for risk-factor clustering may be particularly effective in the early identification of persons likely to develop CVD (Berenson *et al.*, 1998).

Associations were found to change with age in one large prospective study in which authors concluded that "Parental history is an important surrogate measure for cardiovascular risk in the offspring. However, parental history information alone is not sufficient to designate younger children for selective screening for high cholesterol, because of the young age of parents" (Bao *et al.*, 1995). Studies in Canadian Inuit suggest that environmental factors can override an apparently high level of genetic susceptibility to CHD (Hegele, 1999).

From these analyses, authors concluded that the study documented the complexity of the associations between intermediate traits and risk of CAD (Kardia *et al.*, 1998). The results of our study shows that blood lipid and insulin levels of children are likely to differ according to their family history as seen by higher percentages seen in Fig. 1 for diabetes compared to CVD or controls. Furthermore positive family history for diabetes also increases the risk of developing obesity in children. However it could not be ascertained whether genetics or life style factors have a relative contribution in the emergence of these differences as no significant change in diet and lifestyle patterns were seen in the three groups. As diabetes and heart disease are probably two manifestations of an underlying single metabolic derangement i.e Syndrome X, it is possible that the youngsters having positive family history have some underlying physical predisposition to develop any of these two disorders.

Weight-height indices prediction of morbidity and mortality are very reproducible, and appear to be as strongly correlated with risk factor levels as are densitometric estimates of fat mass. (Dietz and Robinson, 1998; Spiegelman *et al.*, 1992). It is important, however, to be aware of the limitations of weight-height indices as surrogate measures for adiposity. Obesity is almost always found to be predictive of higher risk of dyslipidemias and hyperinsulinemia even in childhood and adolescence (Cook and Hurley, 1998; Pinhas *et al.*, 1996; Slyper, 1998).

In studies where impact of lifestyle interventions has been done the interventions were found to be effective in reducing the risk even in children having positive family history for heart diseases or diabetes (Torbus *et al.*, 1996; The Diabetes Prevention Program Research Group, 1999).

Thus on the basis of observations made in this study and similar studies done in others countries the general health education programs should aim at increasing physical activity level of children and encouraging balanced diet in all children regardless of bodyweight or family history. Families with positive history for diabetes or heart disease should be educated to adopt more healthy lifestyles in their offspring.

Subjects with a BMI above the 85th percentile should be considered at risk of overweight and referred to a second level of screening that incorporates additional risk factors, such as family history, total cholesterol, insulin levels and a large increment in BMI over the previous year, plus the adolescent's concern about weight.

Increase in energy intake and decrease in physical activity are the primary environmental influences which need to be reversed. In 45 minutes of exercise, a 165-kg (75-lb) child may be expected to expend 90, 525, 135, and 180 calories during continuous bicycling, running, walking, and dancing, respectively. Clearly, there is a need to balance energy intake with energy output and to introduce activity in place of inactivity. In disease and obesity prevention programs an emphasis on plant-based foods and vegetable and fruit consumption would be a major step forward in avoiding energy-dense foods as seen in another study where 40% of children were taking fast food and cold drinks daily (Hydrie *et al.*, 2004).

Further studies are needed to identify assessment tools that indicate the risk level at which interventions are needed in Pakistani children which would hopefully contribute to future health of Pakistani children.

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