

PREVALENCE OF PLASMA LIPID ABNORMALITIES IN SAUDI CHILDREN

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Background: Lipid levels in children vary in different populations. Due to a close association between high lipid levels and development of atherosclerosis, considerable interest has been directed to investigating lipid levels in children.

Materials and Methods: We conducted this study on 2914 children with ages ranging from 1 year to <15 years, randomly selected during a national household screening program. Fasting blood samples were used for estimation of triglyceride and cholesterol levels.

Results: The overall range for cholesterol was 2.0-5.7 mmol/L and for triglyceride the overall range was 0.1-1.7 mmol/L. The children were separated into 14 groups depending on age, and the cholesterol and triglyceride levels were calculated in each age group. Using published guidelines for estimating "borderline" and "high risk" for coronary artery disease from cholesterol and triglyceride levels, the prevalence of borderline and high-risk groups was calculated. 7.72% of the children fell in the borderline risk group and 1.55% in the high-risk group using cholesterol values, while using triglyceride values, 1.4% and 0.55% fell in the borderline and high-risk groups, respectively. The prevalence of abnormality varied in the different age groups.

Conclusion: The paper discusses the need for a lipid awareness program in Saudi children in an attempt to decrease the complications associated with dyslipidemias during adulthood.

Ann Saudi Med 2001;21(1-2):21-25.

Key Words: Coronary artery disease, cholesterol, triglycerides, dyslipidemia.

Interest in the study of plasma lipids has been at its height during the last one to two decades, due to the close association between high levels of lipids and development of atherosclerosis in children.¹⁻⁸ Lipid levels show differences in different populations and are shown to be affected by age, sex, dietary habits, level of exercise and genetics.⁹⁻²¹ In addition, lipid levels may be affected by the types of food ingested, where food with high saturated fat content tends to elevate the plasma cholesterol levels.^{22,23} In a study by Knuiman et al. in 1983, the plasma cholesterol levels in children around 8-9 years of age, from different countries, were compared.²⁴ The results showed variation in the cholesterol levels in the various countries. The highest cholesterol mean was in children from Finland and the lowest in children from Ghana.²⁴ In a similar study on 13-year-olds in which 15 countries were compared, the highest cholesterol level was in children from Finland and the lowest was in children from Nigeria.²⁵ Several conclusions were drawn from these and other studies. These included the suggestion of geographic pattern in the variation of total cholesterol at specified ages prior to or during puberty.

We conducted this study in an attempt to establish the normal "reference" range for cholesterol and triglyceride in Saudi children aged 1-<15 years, and to determine the prevalence of hypercholesterolemia and hypertriglyceridemia in each age group and in the total group screened. This manuscript presents our results in Saudi children and compares the values obtained with those from other populations.

Materials and Methods

The study population was comprised of apparently healthy Saudi children, who were screened during a household screening program for diabetes mellitus. The screening procedure was statistically designed to be representative of the whole country. The screening procedure divided the regions into different sectors. In randomly selected sectors, every tenth street was selected and on every tenth street every tenth house was enrolled for screening. The telephone numbers were acquired from the local health clinic and the family was contacted. The purpose of the study was explained and the family was invited to join in the study. Only those who volunteered to participate and gave their approval for their inclusion and the inclusion of their children and other family members took part in the study.

On a fixed day, when all family members were requested to remain in a fasting state, an early morning visit was made and blood samples were drawn by venipuncture in heparinized tubes from all children from one to less than

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Accepted for publication 14 March 2001. Received 24 June 2000.

TABLE 1. Mean, median, mode, standard deviation and non-parametric ranges (2.5th-97.5th percentile) for cholesterol and triglycerides in children of different age groups.

Age (years)	No.	Mean (mmol/L)	Median (mmol/L)	Mode (mmol/L)	SD	2.5 th - 97 th percentile
Cholesterol*						
1 - <2	21	3.76	4.2	4.0	1.50	-
2 - <3	89	3.94	4.07	4.8	1.04	1.0-5.3
3 - <4	138	4.14	4.18	4.4	1.0	1.2-5.9
4 - <5	155	3.94	4.04	5.0	0.87	1.5-5.3
5 - <6	179	3.84	3.8	3.8	1.2	1.4-5.9
6 - <7	269	3.82	3.9	4.3	0.91	1.9-5.3
7 - <8	219	4.0	4.16	4.3	0.95	1.6-5.92
8 - <9	320	3.90	3.91	3.4	0.98	1.7-5.6
9 - <10	235	3.95	3.9	3.9	1.03	1.1-5.6
10 - <11	292	3.95	4.01	4.7	0.93	1.6-5.4
11 - <12	233	3.87	3.94	3.6	1.1	1.3-5.8
12 - <13	268	3.91	3.96	3.2	0.94	1.5-5.5
13 - <14	198	3.75	3.70	3.2	1.0	1.5-5.7
14 - <15	298	3.62	3.70	4.1	0.9	1.5-5.2
Triglycerides**						
1 - <2	21	0.88	0.71	0.71	0.48	-
2 - <3	89	1.0	0.9	0.9	0.50	0.26-2.2
3 - <4	138	0.78	0.73	0.9	0.39	0.2-1.81
4 - <5	155	0.88	0.77	0	0.9	0.26-1.9
5 - <6	179	0.82	0.7	0.7	0.54	0.2-2.0
6 - <7	269	0.77	0.64	0.6	0.46	0.2-2.08
7 - <8	219	0.81	0.73	0.70	0.49	0.20-2.48
8 - <9	320	0.7	0.7	0.40	0.40	0.25-1.9
9 - <10	235	0.72	0.7	0.7	0.43	0.14-1.67
10 - <11	292	0.73	0.67	0.73	0.4	0.16-1.61
11 - <12	233	0.75	0.7	0.6	0.4	0.17-1.7
12 - <13	268	0.87	0.74	0.6	0.5	0.18-2.18
13 - <14	198	0.84	0.78	0.7	0.51	0.18-2.1
14 - <15	298	0.81	0.7	0.7	0.52	0.15-2.19

*ANOVA for cholesterol: F=3.528; P<0.0001; **ANOVA for triglycerides: F=4.155; P<0.0001.

TABLE 2. Prevalence of cholesterol and triglycerides elevation in the total number of Saudi children investigated.

	Total no. investigated	Borderline risk		High risk		Total risk	
		No.	%	No.	%	No.	%
Cholesterol	2914	231	7.72	43	1.55	274	9.4
Triglycerides	2914	41	1.4	16	0.55	57	1.96

fifteen years of age. Only 21 children who were <2 years were included for blood extraction, and they had been fasting for 4-6 hours. The total group comprised 2914 children and adolescents between 1-15 years of age. The fresh blood was centrifuged to separate the plasma from the cells and the plasma was stored frozen until required for analysis. The cholesterol and triglycerides were measured using Autoanalyzer, American Monitor "Parallel" at King Khalid University Hospital, King Saud University, Riyadh. This estimates cholesterol by the cholesterol esterase method, while triglyceride estimation depends on measuring a lipase assay. The data were entered into computer at the Computer Centre, King Saud University, and analyzed using the Statistical Analysis System (SAS) Program. The mean, median, mode, standard deviation,

skewness, kurtosis, percentile range, frequency distribution histogram and normal probability plots were obtained for the total child population. The child population was further grouped according to age into 14 groups and the level of cholesterol and triglycerides were separately analyzed for each group.

To compare the results of any two groups, Student's *t*-test was used and *P*<0.05 was considered statistically significant. For comparison of the results of several groups ANOVA was used and *P*<0.05 was considered statistically significant.

Results

The mean and standard deviations for cholesterol and triglycerides in the total child group screened were 3.9±0.9 mmol/L and 0.8±0.48 mmol/L, respectively. The frequency distribution histogram and normal probability plot for cholesterol for the overall Saudi children were obtained and showed the cholesterol distribution as normal Gaussian distribution with a slight skewness of 0.3 and kurtosis of 0.2 and a straight line for normal probability plot. The parametric range (mean±2SD) was 2.0-5.7 mmol/L and the nonparametric range (2.5th-97.5th percentile) was 1.8 to 5.6 mmol/L. The results of mean, median, mode and standard deviation in different age groups, and the parametric and nonparametric ranges, are presented in Table 1. The highest mean was in the 3-4-year-olds and a significant decrease occurred in the mean cholesterol with age, with the lowest mean in those 14-15 years old (ANOVA: F=3.528; *P*<0.0001).

For triglycerides, the frequency distribution showed a normal Gaussian distribution with a skewness of 1.0 and kurtosis of 1.2. The normal probability plot was a straight line. The overall parametric range (mean±2SD) was 0.1-1.7 mmol/L, while the percentile range was 0.3-1.7 mmol/L. The results of mean, median, mode, standard deviation and parametric and nonparametric ranges (2.5th-97.5th percentile) for triglyceride levels in the different age groups are presented in Table 1. Significant variations in the mean values and ranges were seen in the levels of triglyceride in children in different age groups (ANOVA: F=4.155; *P*<0.0001). The highest level of triglyceride was in the 2-3 year olds and the lowest level in those from 8 to 11 years. A slight but nonsignificant increase was observed beyond this age.

Using the normal values of cholesterol and triglycerides quoted by Kuitrovich²⁶ (for cholesterol, desirable, borderline and high-risk values were <4.36 mmol/L, 4.36-4.88 mmol/L and ≥5.13 mmol/L, respectively, while for triglycerides the desirable, borderline and high-risk values were <0.825 mmol/L, 0.825-1.089 mmol/L and ≥1.1 mmol/L), the prevalence of borderline and high-risk cases was obtained and the prevalence of cholesterol and triglyceride elevation in the total child group was calculated (Table 2). The prevalence of cholesterol and triglyceride elevation was also calculated for each age group and the results of borderline risk and high-risk cases determined, as

TABLE 3. Prevalence of cholesterol and triglycerides elevation in Saudi children in different age groups.

Age (years)	Total no. investigated	Cholesterol level (mmol/L)				Total risk
		Borderline risk 4.36-4.88		High risk ≥ 5.13		
		No.	%	No.	%	
Cholesterol						
1 - <2	21	1	4.76	0	0	4.76
2 - <3	89	2	2.25	0	0	2.25
3 - <4	138	13	9.42	4	2.89	12.32
4 - <5	155	7	4.51	1	0.64	5.16
5 - <6	179	17	9.49	4	2.23	11.73
6 - <7	269	10	3.71	5	1.86	5.57
7 - <8	219	28	12.78	2	0.91	13.69
8 - <9	320	35	10.94	8	2.50	13.43
9 - <10	235	30	12.76	4	1.70	14.47
10 - <11	292	18	6.16	6	2.05	8.22
11 - <12	233	24	10.3	1	0.43	10.73
12 - <13	268	24	8.96	1	0.37	9.33
13 - <14	198	13	6.56	6	3.03	9.59
14 - <15	298	9	3.0	1	0.33	3.36
Triglycerides						
1 - <2	21	0	0	0	0	0
2 - <3	89	1	1.12	0	0	1.12
3 - <4	138	3	2.17	6	4.35	6.52
4 - <5	155	3	1.94	1	0.65	2.58
5 - <6	179	4	2.23	0	0	2.23
6 - <7	269	1	0.59	2	0.74	1.1
7 - <8	219	2	0.9	0	0	0.9
8 - <9	320	2	0.63	0	0	0.63
9 - <10	235	1	0.43	0	0	0.43
10 - <11	292	3	1.03	0	0	1.03
11 - <12	233	2	0.86	0	0	0.86
12 - <13	268	9	3.36	6	2.24	5.59
13 - <14	198	5	2.53	0	0	2.53
14 - <15	298	5	1.68	1	0.34	2.01

presented in Table 3. For cholesterol the highest prevalence of elevation was in the 7-10-year age group, while for triglycerides the highest prevalence of elevation was in the 3-4-year and 12-13-year age group.

Discussion

The increasing evidence that atherosclerosis has its beginning in childhood has also directed the attention towards the cholesterol levels in children, since it is shown that the beginning of fatty streaks in arteries occurs during childhood, leading to the development of advanced atherosclerotic lesions in adults.^{4,27,28} In recent years, serum cholesterol has been the third nationally recommended health screening test in the US population and is highly recommended by the National Heart, Lung and Blood Institute²⁹ for both adults and children.²⁹⁻³¹

Total cholesterol and triglycerides levels are affected by age, sex, lifestyle, diet, infections, alcohol consumption, caffeine intake, contraceptive use, and cigarette smoking.^{32,33} Factors such as obesity, height, dietary changes and changes in exercise routines can influence both pediatric and adult lipid levels.^{13-15,27-38} Several

screening studies have been reported in children of different ages and in different populations.^{11,15-19}

This study has fulfilled several aims, including: 1) to establish normal reference values for cholesterol and triglycerides in Saudi children and adolescents; 2) to compare this data with results published in the literature for other populations; and 3) to determine the frequency of hypercholesterolemia and hypertriglyceridemia. The results of this study show that cholesterol levels in Saudi children are lower than those reported for the populations of Finland, New Zealand and Italy, are similar to the Philippine population and higher than the population in some of the African countries²⁴ (Table 4).

The differences between populations may be a consequence of several factors, including genetic and environmental factors, dietary habits, lifestyle, etc. During the last few decades, changes in the lifestyle of the Saudi population have been very obvious. Fast food restaurants have increased in number and fast foods have become a very popular component of everyday life. This could account for the high prevalence of cholesterol elevation in the children of different ages.

Over 9% of all Saudi children and over 10% of those between 3-14 years of age, fall in the high-risk group for coronary artery disease (CAD) development when cholesterol levels are used. Increased levels of plasma total cholesterol are a strong predictor of CAD in adults.²⁷⁻²⁹ Though the link between lipid levels in childhood and CAD in middle age has not been proven unequivocally, the significant association between cholesterol levels in childhood and those in the third decade supports the link between cholesterol and atherosclerosis starting early in life.^{2-10,22}

In this study, hypertriglyceridemia was not seen as a major problem. Only 1.96% of the total children fell in that risk group. Fluctuations are seen in the different groups and in the 3-4 years and 12-13 years the prevalence is more than 5%. Whether elevated levels of plasma total triglycerides are an independent predictor in CAD is controversial, however, hypertriglyceridemia is present in many patients with premature CAD.

The significant changes in plasma lipids seen during adolescence in this study may result from sexual maturation and related hormone levels and alteration in weight and height associated with pubertal changes. Physical fitness also influences lipid levels, where it was shown that boys who were physically fit had lower levels of cholesterol and triglycerides than the non-fit boys.^{24,25,39} Similarly, the extent of physical activity plays an important role in decreasing total cholesterol, triglycerides and LDL cholesterol and increasing HDL cholesterol.^{13,14,21}

We propose a lipid awareness program in Saudi children with universal screening for dyslipidemia (particularly hypercholesterolemia), overweight and obesity, in order to provide health counselling to decrease the relative risk of CAD development in later life.³⁵ This can be first done in schools and screening conducted once every few years should suffice. These steps will help

TABLE 4. Cholesterol and triglyceride levels reported in the literature.²⁴

Population	Sex	Age group (years)	No. investigated	Cholesterol (mmol/L) Mean±SD (range)	Significance compared to results in Saudis**
Finland	M+F	9.1±0.6	133	4.9±0.8	t=12.59 P<0.0001
New Zealand	M+F	9.1±0.5	117	4.5±0.7	t=7.125 P<0.0001
Italy	M+F	9.0±0.7	109	4.1±0.9	t=2.28 P<0.023
Philippines	M+F	8.8±0.5	114	3.8±0.6	NS
Ghana	M+F	8.9±0.6	116	3.3±0.7	t=7.095 P<0.0001
Saudi Arabia*	M+F	9.7±3.9	2914	3.9±0.9	—

*Current study; NS=nonsignificant.

achieve better health for Saudis. The advice of the National Heart, Lung and Blood Institute to the American public to “know your numbers” is accepted by millions of Americans.²⁹ In fact, cholesterol screening is conducted in physicians’ offices using instruments that provide reliable results that can be immediately interpreted by the physician himself.^{30,34} There is a need for such screening in Saudi children, particularly since Saudi lifestyle and eating habits are drastically changing and overweight and obesity prevalence is fast increasing. A well-designed national cholesterol education program in Arabic is also required to improve awareness. In addition, family counselling is necessary to improve dietary habits of the children. These steps may be just a few in improving health status of Saudis in the new millennium.

References

- Newman WP III, Freedman DS, Voors AW, et al. Relationship of serum lipoprotein levels and systolic blood pressure to early atherosclerosis. The Bogalusa Heart Study. *N Engl J Med* 1986;314:128-44.
- Freedman DS, Newman WP III, et al. Black-white differences in aortic fatty streaks in adolescence and early adulthood. The Bogalusa Heart Study. *Circular* 1988;77:856-64.
- Stasy HC. Evolution and progression of atherosclerotic lesions in coronary arteries of children and young adults. *Arteriosclerosis* 1989;9(Suppl 1):1-9.
- Strong WB, ed. *Atherosclerosis: its pediatric aspects*. New York: Grune and Stratton, 1991.
- Washino K, Takada H, Nagashima M, Iwata H. Significance of the atherosclerogenic index and body fat in children as markers for future, potential coronary heart disease. *Pediatr Int* 1999;41:260-5.
- Berenson GS, Srinivasan SR, Bao W, Newman WP, Tracy RE, Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. *N Engl J Med* 1998;338:1650-6.
- Rabelo LM, Viana RM, Schimith MA, Patin RV, Valverde MA, Denadai RC, et al. Risk factors for atherosclerosis in students of a private university in Sao Paulo, Brazil. *Arq Bras Cardiol* 1999;72:569-80.
- Chen W, Bao W, Begum S, Elkasabany A, Srinivasan SR, Berenson GS. Age-related patterns of the clustering of cardiovascular risk variables of syndrome X from childhood to young adulthood in a population made up of black and white subjects: the Bogalusa Heart Study. *Diabetes* 2000;49:1042-8.
- Tejada C, Strong JP. Distribution of coronary aortic atherosclerosis by geographic location, race and sex. *Lan Invest* 1968;18:509-26.
- McGill HC Jr. *The geographic pathology of atherosclerosis*. Baltimore: Williams & Wilkins Co., 1968.
- Cowin I, Emmett P. Cholesterol and triglyceride concentrations, birthweight and central obesity in pre-school children. ALSPAC Study Team. *Avon Longitudinal Study of Pregnancy and Childhood. Int J Obes Relat Metab Disord* 2000;24:330-9.
- Sothern MS, Despinasse B, Brown R, Suskind RM, Udall JN, Blecker U. Lipid profiles of obese children and adolescents before and after significant weight loss: differences according to sex. *South Med J* 2000;93:278-82.
- Tolfrey K, Jones AM, Campbell IG. The effect of aerobic exercise training on the lipid-lipoprotein profile of children and adolescents. *Sports Med* 2000;29:99-112.
- Katzmarzyk PT, Malina RM, Bouchard C. Physical activity, physical fitness, and coronary heart disease risk factors in youth: the Quebec Family Study. *Prev Med* 1999;29:555-62.
- Freedman DS, Dietz WH, Srinivasan SR, Berenson GS. The relation of overweight to cardiovascular risk factors among children and adolescents: the Bogalusa Heart Study. *Pediatrics* 1999;103:1175-1182.
- Tolfrey K, Campbell IG, Jones AM. Intra-individual variation of plasma lipids and lipoproteins in prepubescent children. *Eur J Appl Physiol Occup Physiol* 1999;79:449-56.
- Hickman TB, Briefel RR, Carroll MD, Rifkind BM, Cleeman JI, Maurer KR, Johnson CL. Distributions and trends of serum lipid levels among United States children and adolescents ages 4-19 years: data from the Third National Health and Nutrition Examination Survey. *Prev Med* 1998;27:879-90.
- Ku CY, Gower BA, Nagy TR, Goran MI. Relationships between dietary fat, body fat, and serum lipid profile in prepubertal children. *Obes Res* 1998;6:400-7.
- Brotons C, Ribera A, Perich RM, Abrodos D, Magana P, Pablo S, et al. Worldwide distribution of blood lipids and lipoproteins in childhood and adolescence: a review study. *Atherosclerosis* 1998;139:1-9.
- Takada H, Harrell J, Deng S, Bandgiwala S, Washino K, Iwata H. Eating habits, activity, lipids and body mass index in Japanese children: the Shiratori Children Study. *Int J Obes Relat Metab Disord* 1998;22:470-6.
- Meininger JC, Hayman LL, Coates PM, Gallagher PR. Genetic and environmental influences on cardiovascular disease risk factors in adolescents. *Nurs Res* 1998;47:11-8.
- Holman R. Atherosclerosis: a pediatric nutrition problem. *American J Clin Nutr* 1961;9:565-9.
- Leis R, Pavon P, Queiro T, Recarey D, Tojo R. Atherogenic diet and blood lipid profile in children and adolescents from Galicia, NW Spain. The Galinut Study. *Acta Paediatr* 1999;88:19-23.
- Knuiman JT, Westenbrink S, Van der Heyden, et al. Determinant of total and high density lipoprotein cholesterol in boys from Finland, the Netherlands, Italy, the Philippines and Ghana with special reference to diet. *Hum Nutr Clin Nutr* 1983;3237-54.
- Wynder EL, Williams CL, Laakso K, Levenstein M. Screening for risk factors for chronic disease in children from fifteen countries. *Prev Med* 1981;10:121-32.
- Kuiterovich PO Jr. *Beyond cholesterol: the Johns Hopkins Complete guide for avoiding heart diseases*. Baltimore: The Johns Hopkins Press, 1989.
- Solberg LA, Strong JP. Risk factors and atherosclerosis lesion: a review of autopsy studies. *Atherosclerosis* 1983;3:187-98.

28. Strong JP, McGill HC. The natural history of coronary atherosclerosis. *Am J Pathol* 1962;40:37-49.
29. National Institute of Health Consensus Development Conference Statement. Lowering blood cholesterol to prevent heart disease. Albany, NY: New York State Department of Health and Human Services, Public Health Services, 1985.
30. Cleeman JI. The National Cholesterol Education Program. *Clin Lam Med Cholesterol Screening* 1989;9:7-16.
31. Gillum RF. Distribution of waist-to-hip ratio, other indices of body fat distribution and obesity and associations with HDL cholesterol in children and young adults aged 4-19 years: The Third National Health and Nutrition Examination Survey. *Int J Obes Relat Metab Disord* 1999;23:556-63.
32. Webber LS, Hunter SM, Johnson CC, et al. Smoking alcohol and oral contraceptives – effects on lipids during adolescence and young adulthood – Bogalusa Heart Study. *Ann N Y Acad Sci* 1991;623: 135-54.
33. Laner RM, Lee J, Carte WR. Factors affecting the relationship between childhood and adult cholesterol: the Muscatine study. *Pediatrics* 1988;82:309-18.
34. Liu CS, Lin CC, Shih HC, Li TC. The advisability of implementing cholesterol screening in school-age children and adolescents with a family history of cardiovascular disease and hyperlipidaemia. *Fam Pract* 1999;16:501-5.
35. Morrison JA, Barton BA, Biro FM, Daniels SR, Sprecher DL. Overweight, fat patterning, and cardiovascular disease risk factors in black and white boys. *J Pediatr* 1999;135:451-7.
36. Kayatekin BM, Semin I, Acarbay S, Oktay G, Selamoglu S. A comparison of the blood lipid profiles of professional sportspersons and controls. *Indian J Physiol Pharmacol* 1998;42:479-84.
37. Schmidt GJ, Stensel DJ, Walkuski JJ. Blood pressure, lipids, lipoproteins, body fat and physical activity of Singapore children. *J Paediatr Child Health* 1997;33:484-90.
38. Chu NF, Rimm EB, Wang DJ, Liou HS, Shieh SM. Relationship between anthropometric variables and lipid levels among school children: the Taipei Children Heart Study. *Int J Obes Relat Metab Disord* 1998;22:66-72.
39. Kuitrovich PO Jr. Plasma lipids and lipoprotein levels in childhood. *Ann N Y Acad Sci* 1991;623:90-107.