Thematic Article

Cardiovascular risk in the Asia–Pacific region from a nutrition and metabolic point of view: lipid

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Hypercholesterolemia, especially low-density lipoprotein cholesterol, is well-known as a risk factor for coronary heart disease. The prevalence of hyperlipidemia in the Asia–Pacific regions, although not as high as in the North American and European regions, in adults and children varied from country to country. The 'Cardiovascular Risk Factor of Chiang Mai children (CARFACC)' study has shown the small 'n' and capital 'N' phenomenons, where in some individuals, blood lipid levels were tracked from childhood to adulthood. The new concept of programming by early nutrition on later adult health has now been accepted. The prevention of dyslipidemia during childhood should receive more attention.

Key words: Asia–Pacific, cardiovascular disease risk, hypercholesterolemia, lipid.

Introduction

Hypercholesterolemia is one of the major established risk factors for coronary heart disease (CHD), with CHD being one of the five leading causes of death in the Asia–Pacific countries.[1] Hypercholesterolemia is affected by genetic, diet, disease state and environmental factors. Recently, attention has been focused on the nutritional programming in perinatal period and the diseases in adulthood such as cardiovascular disease, atherosclerosis, blood lipids and osteoporosis. Human evidence supporting nutritional programming has major potential biological and medical significance. Currently, there are many published papers on the relationship between lipid and cardiovascular disease. However, the reviews on this aspect in some developing countries, especially in the Asia–Pacific region, are few. The prevalence of hyperlipidemia both in children and adults varies from country to country, depending on their dietary intakes, diets during perinatal period and early childhood, socioeconomic status, lifestyle behaviour, race, age, sex, and also the criteria used. This paper reviews the relationship between lipid and cardiovascular disease in the Asia–Pacific region.

Prevalences of dislipidemia in adults and children in the Asia–Pacific region

The prevalence of high total cholesterolemia (TC) in children is not well-defined as there are problems in selecting the upper limit cut-off level for normal TC in children. The prevalence of so-called 'high TC' in children therefore varies from country to country according to the cut-off level selected. The prevalence of serum TC above 180 mg/dL and 240 mg/dL varies from 5 to 24% for US and 8 to 39% for Finland (Table 1[2–9]). In the Bogalusa Heart Study the prevalence of white children with a triglycerides (TG) value above 136 mg/dL was 5%.[2] Lauer *et al.* found that 8% of children aged 6–18 years had TG levels above 100 mg/dL.[3] In Australia, it was found that 10% of adolescents aged 15 years had fasting serum TG levels above 1.16 mmol/L for males and 1.26 mmol/L for females.[4] In the Asia–Pacific regions, the prevalences of serum TC above the selected cut-off levels are shown in Table 2[10–21] for adults and Table 3[22–27] for children.

Tracking of blood lipids from childhood to adulthood

Considerable tracking of lipid and lipoprotein levels in children occurs in a general population. Tracking is a measure of the tendency of an individual to maintain a rank relative to their peers through time. That is, serum lipid and lipoprotein determinations have considerable value in predicting future concentrations, especially when based on repeat determinations. There is little evidence that serum lipid level at birth is predictive of the level at 6 months or 1 year.[28] However, by 6 months, 30% of children who were above the 90th centile for TC at this time tended to remain in the top decile at 1 year and 61% were in the top three deciles. Tracking was most pronounced for low-density lipoprotein cholesterol (LDLC) for which 40% of those who were in the top decile at 6 months remained in the top three deciles at 1 year. This tendency to track was also noted at the lower end of the distribution. Table 4 shows correlation coefficients of serum TC and TG from the Bogalusa Heart Study. It appears that correlation coefficients are highest for TC for 4-year-olds versus 6-year-olds ($r = 0.7$) with r-values of 0.6–0.7 for 1-year-olds versus 4-year-olds and also for 1-year-olds versus

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Table 1. Prevalence (%) of serum TC above 180–240 mg/dL in children in United States and Finland

Countries	Cut-off levels (mg/dL)	Age (years)	Percent above cut-off levels		
			Boys	Girls	Both sexes
United States[2,3,5–7]	180	11–14	–	–	17
	200	8–12	20	–	–
	200	6–18	24	–	–
	205	6–17	–	–	5
	210	5–14	–	–	5
Finland[8,9]	192	3–18	–	–	39
	211	3–18	–	–	9
	230	3–18	–	–	8
	230	13–15	9	13	–

TC: 1 mg/dL = 0.026 mmol/L.

Table 2. Prevalence (%) of serum TC above cut-off levels in adults in the Asia–Pacific region

Country	Age (years)	Cut-off levels (mmol/L)	% TC above cut-off levels
Australia[10]	30–60	5.5	51.8 (m); 39.6 (f)
Hong Kong[11]	30–60	5.2	54.2
India[12]	20–73	5.2	22
Indonesia[13]	25–64	6.5	13.4
New Zealand[14]	30–69	7.5	8.0
Papua New Guinea[15]	> 25	5.2	16.0 (rural); 56.0 (urban)
Singapore[16]	30–69	6.5	23.7
South Korea[17]	35–59	240 mg/dL	8.9 (m); 10.4 (f)
Sri Lanka[18]	35–59	6.5	12.6
Thailand[19–21]	> 30	6.2	12.2 (m); 16.9 (f)
	> 25	200 mg/dL	20.0 (m); 62.0 (f) (high SES)
	Postmeno	200 mg/dL	91.3

m, male; f, female. Postmeno, postmenopausal women; SES, socioeconomic status.

Table 3. Prevalence (%) of serum TC above cut-off levels in children in the Asia–Pacific region

Country	Age (years)	Cut-off levels (mg/dL)	% TC above cut-off levels	
			Boys	Girls
Australia[4,10,22]	14–15	4.96 (mmol/L)	12.4	–
		5.4 (mmol/L)	–	9.0
		173	23	40
	11–18	200	28	–
		240	12	–
	15	200	5	15
	12	213	10	10
Pakistan[23]	5–19	4.4 (mmol/L)	22	33
Taiwan[24]	5–19	170	36.5	39.7
Thailand[25–27]	0–72	170	27	19
	9–18	170	40.2	47.2
	6–15	170	44.0	56.0

Table 4. Correlation coefficients by age and year of follow-up for serum cholesterol and triglycerides in children: Bogalusa Heart Study, 1973–1979

Age (years)	*n*	TC			*n*	TG		
		1 vs 4	1 vs 6	4 vs 6		1 vs 4	1 vs 6	4 vs 6
2–4	379	0.57	0.59	0.72	285	0.27	0.17*	0.28
5–6	451	0.66	0.62	0.70	352	0.30	0.34	0.44
7–8	407	0.69	0.67	0.75	335	0.37	0.36	0.45
9–10	386	0.70	0.69	0.70	287	0.34	0.41	0.50
11–12	351	0.64	0.61	0.74	234	0.25	0.30	0.47
13–14	184	0.73	0.64	0.72	114	0.40	0.35	0.41

TC, serum cholesterol; TG, triglycerides. *$P < 0.005$; all, $P < 0.0001$. Source: Parker FC, Harsha DW, Farris RP, Webber LS, Frank GC, Berenson GS. Reducing the risk of cardiovascular disease in children. In: Holroyd KA, Creer TL, eds. Self-management of chronic disease. Handbook of clinical interventions and research. Orlando: Academic Press, 1986.

6-year-olds. The *r*-values do not increase with age. The findings are similar for TG but with lower *r*-values. Such correlations for TC indicate that even one serum TC determination has high predictive value for subsequent levels.

Lauer *et al.* in a 15-year follow-up study of 2446 schoolchildren from Muscatine, Iowa found that the correlation coefficients between childhood and adulthood TC and LDLC levels are 0.5–0.6 (Table 5).[29] The data show a significant correlation between TC and LDLC at 7–8 years and 20–25 years of age, as well as between the levels at 13–14 and 26–30 years of age. For high-density lipoprotein cholesterol (HDLC) the *r*-values are very low. Those children with childhood TC level above 90th percentile had a 24–32% risk of developing high levels at 20 years of age or thereafter.

Programming by early nutrition

There is growing evidence of an increasing complex and multifactorial etiology of heart diseases. It seems likely that the large geographical variations in cardiovascular disease morbidity and mortality, even though at least partly genetic in origin, are influenced by a factor acting prenatally and in early life, or by a combination of factors present throughout the lifespan. Changes in fetal growth pattern have been related to adult disease risk and there are many theories about the underlying mechanisms affecting cell division during critical periods of tissue development.[30] Evidence for programming by nutrition is established in animals, in whom brief pre- or postnatal nutritional manipulations may program adult size, metabolism, blood lipids, diabetes, blood pressure, obesity, atherosclerosis, learning, behaviour and lifespan.[31] Human epidemiological data link potential markers of early nutrition (size at birth or in infancy) to cardiovascular disease and its risk factors in adulthood.[32] Low bodyweight, head circumference and ponderal index at birth and low weight at aged 1 year have been associated with an increased risk of later cardiovascular disease. Small size at birth and to 1-year-old has also been associated with higher blood pressure and adverse changes in plasma concentrations of glucose, insulin, fibrinogen, factor VII and apolipoprotein B; abdominal circumference at birth is inversely associated with higher serum concentration of total cholesterol, LDL cholesterol and apolipoprotein B.[32] Tienboon *et al.* found that children who consumed cod liver oil in their early life (during their preschool years) had body mass index (BMI), waist-to-hip ratio (WHR), abdominal circumference (AC), supra-iliac skinfold (SISF) thickness (and a trend for total cholesterol) lower than those children who did not consume.[33] It seems that humans have sensitive windows for nutrition in terms of later outcomes; for instance, perinatal diet influences neurodevelopment and bone mineralization into mid-childhood. Possible biological mechanisms for storing throughout life the 'memory' of early nutritional experience and its expression in adulthood include adaptive changes in gene expression, preferential clonal selection of adapted cells in programmed tissues and programmed differential proliferation of tissue cell types. Animal and human evidence supporting nutritional programming has major potential biological and medical significance.[31]

Table 5. Correlation coefficients between plasma TC level in childhood and adult TC, LDLC and HDLC levels

Variable	Sex	Adult age in years	
		20–25[a]	26–30[b]
TC	M	0.56	0.52
	F	0.64	0.52
LDLC	M	0.56	0.50
	F	0.65	0.49
HDLC	M	*NS*	*NS*
	F	*NS*	0.11

All $P < 0.05$; *NS*, non-significant; TC, serum cholesterol; LDLC, low-density lipoprotein cholesterol; HDLC, high-density lipoprotein cholesterol; a, childhood measurement at 7–8 years of age; b, childhood measurement at 13–14 years of age.

The 'Cardiovascular Risk Factor of Chiang Mai Children' (CARFACC) study: the small 'n' and capital 'N' phenomenons

The CARFACC study is planned to be a prospective longitudinal study conducted by Tienboon (1995) in 1234 randomly selected children aged 6–16 years in Chiang Mai, Thailand.[34] It measured the cardiovascular risk factors of children from well-to-do families. The children were followed-up every 10 years. At the beginning of the study, it was found that the prevalence of high TC according to age showed a small 'n' phenomenon in boys and a capital 'N' phenomenon in girls. In boys, the prevalence of serum TC level above the cut-off level (170 mg/dL) decreases from 6 years (74%) to a lower value (40%) at 9 years and increases again to a higher value (72%) at 11 years and then declines to the age 15–16 years (13%, small 'n' phenomenon). Whereas in girls, the prevalence increases from 6 years (57%) to a higher value (81%) at 9 years and decreases to 35% at the age around 11–13 years and then increases to 15–16 years (60%, capital 'N' phenomenon). The CARFACC study not only showed the high prevalence of elevated TC level in children from well-to-do families but also a high prevalence of obesity (varies with age, weight-for-height (W/H) > 120%) in boys (6–28%) and girls (11–26%) with more prevalence in boys than in girls.

The Geelong Adolescent Health Study (GAHS)

The GAHS study is set out to determine the relative contribution of early environment, parental and contemporary influences on body size, fatness and coronary heart disease risk in adolescence.[10] The study was a retrospective longitudinal study of 213 families. The relevant data on 14- to 15-year-old adolescents and their parents were obtained and linked with data previously obtained in infancy and early childhood in the same individuals from infant welfare centre and school medical records. The findings of the GAHS study confirmed the important role of early environment both in relation to body size and fatness and to CHD risk factor status in adolescence. The study also confirmed the importance of parental risk factor status on adolescent risk factor status particularly with respect to smoking and TC level. If both parents had TC values at or above 5.5 mmol/L (Table 6), the adolescent was at significantly higher risk for TC above 90th percentile for age and sex (relative risk 6.2; CI 2.3–16.5). Of the variables measured, the most significant influences on CHD risk factor status in adolescence were:

(1) weight at 50 months for systolic blood pressure (SBP) in adolescence,

Table 6. Adolescent serum total cholesterol level relative to parents' cholesterol level[a]

Parents' cholesterol category	Adolescent's cholesterol category		
	> 90th centile[b]	< 90th centile[b]	Total
Both >5.5 mmol/L	11	22	33
One >5.5 mmol/L	5	88	93
Total	16	110	126

a, relative risk for elevated cholesterol = 6.2, 95% CI 2.3–16.5; b, of a national sample of Australian adolescents.[4]

(2) height at 80 months and serum TC of fathers and mothers for TC,
(3) BMI at 80 months for WHR, and
(4) parental smoking habits for adolescent smoking.

Conclusion

In conclusion, prevention of dyslipidemia during childhood is crucial. More attention should be now focused on the effect of programming by early nutrition on later adult health.

References

1. International Medical Foundation of Japan. Asia Pacific Food Industry, January/February, 2000; 1: 2–6.
2. Frerichs RR, Srinivasan SR, Webber LS, Berenson GS. Serum cholesterol and triglyceride levels in 3446 children from a biracial community. Circulation 1976; 54: 302–309.
3. Lauer RM, Connor WE, Leaverton PE, Reiter MA, Clarke WR. Coronary heart disease risk factors in school children: the Muscatine study. J Pediatr 1975; 86: 697–706.
4. Australian Council for Health Physical Education and Recreation (ACHPER) (ed.). Australian health and fitness survey 1985: the fitness, health and physical performance of Australian school students aged 7–15 years. Adelaide: Australian Council for Health, Physical Education and Recreation, 1987.
5. William CL, Arnold CB, Wynder EL. Primary prevention of chronic disease beginning in childhood. The know your body program: design of study. Prev Med 1977; 6: 344–357.
6. Wilmore JM, McNamara JJ. Prevalence of coronary heart disease risk factors in boys, 8–12 years of age. J Pediatr 1974; 84: 527–533.
7. Morrison JA, de Groot I, Edwards BK. Lipids and lipoproteins in 927 school children, ages 6–17 years. Pediatrics 1978; 62: 990–995.
8. Viikari J, Akerblom HK, Uhari M. Atherosclerosis precursors in Finnish children and adolescents. In: Hetzel B, Berenson GS (eds). Cardiovascular risk factors in childhood: epidemiology and prevention. Amsterdam: Elsevier Science Publishers, 1987; 21–42.
9. Puska P, Vartiainen E, Pallonen U. The North Karelia Youth Project. A community-based intervention study on CVD risk factors among 13- to 15-year-old children: Study design and preliminary findings. Prev Med 1981; 10: 133–148.
10. Tienboon P, Rutishauser IH, Wahlqvist ML. A family study of coronary risk factors in Geelong. Aust J Pub Hlth 1992; 16: 20–25.
11. Chan WK, Chiu A, Ko GT, Wu MF, Liu FL, Choi KW. Ten-year cardiovascular risk in a Hong Kong population. J Cardiovasc Risk 1999; 6: 163–169.
12. Gupta R, Gupta HP, Kumar N, Joshi AK, Gupta VP. Lipoprotein lipids and the prevalence of hyperlipidaemia in rural India. J Cardiovasc Risk 1994; 1: 179–184.
13. Boedhi-Darmojo R, Setianto B, Sutedjo D, Kusmana D, Andradi M, Supari F, Salan R. A study of baseline risk factors for coronary heart disease: results of population screening in a developing country. Rev Epidemiol Sante Publique 1990; 38: 487–491.
14. McMenamin JP. Screening for coronary heart disease risk among men in a general practice. NZ Med J 1995; 108: 167–168.
15. Hodge AM, Dowse GK, Erasmus RT, Spark RA, Nathaniel K, Zimmet PZ, Alpers MP. Serum lipids and modernization in coastal and highland Papua New Guinea. Am J Epidemiol 1996; 144: 1129–1142.
16. Hughes K, Aw TC, Choo MH. Hypercholesterolaemia and its treatment in Singapore with implications for screening. Ann Acad Med Singapore 1997; 26: 449–452.
17. Jee SH, Appel LJ, Suh I, Whelton PK, Kim IS. Prevalence of cardiovascular risk factors in South Korean adults: results from the Korea Medical Insurance Corporation (KMIC) Study. Ann Epidemiol 1998; 8: 14–21.
18. Mendis S, Ekanayake EM. Prevalence of coronary heart disease and cardiovascular risk factors in middle aged males in a defined population in central Sri Lanka. Int J Cardiol 1994; 46: 135–142.
19. Tatsanavivat P, Klungboonkrong V, Chirawatkul A, Bhuripanyo K, Manmontri A, Chitanondh H. Prevalence of coronary heart disease and major cardiovascular risk factors in Thailand. Int J Epidemiol 1998; 27: 405–409.
20. Linpisarn S, Tienboon P, Laokuldilok J, Promtet N, Wongworapat K, Santawanpat S, Dewier M, Suskind R, Fuchs G. Coronary risk factor in adults: hyperlipidemia. Chiang Mai Med Bull 1994; 33: 76–77.
21. Taechakraichana N, Pasatrat S, Ninlagarn T, Panyakhamlerd K, Chaikittisilpa S, Limpaphayom K. Dyslipidemia among healthy postmenopausal Thai women. J Med Assoc Thai 1999; 82: 895–899.
22. Hickie JB, Sutton J, Russo P, Ruys J, Kraegen EW. Serum cholesterol and serum triglyceride levels in Australian adolescent males. Med J Aust 1974; 1: 825–828.
23. Badruddin SH, Molla A, Khurshid M, Vaz S, Hassanali S. Cardiovascular risk factors in school children from low middle income families in Karachi, Pakistan. JPMA J Pak Med Assoc 1994; 44: 106–112.
24. Lin CC, Lai MM, Liu CS, Li TC. Serum cholesterol levels and prevalence of hypercholesterolemia in school-aged Taiwanese children and adolescents: the Taichung Study. Chung Hua I Hsueh Tsa Chih (Taipei) 1999; 62: 787–794.
25. Tienboon P, Linpisarn S, Laokuldilok J, Promtet N. Blood cholesterol level of preschool children. Chiang Mai Med Bull 1995; 34: 64.
26. Suthutvoravut U, Charoenkiatkul S, Chitchumroonchokchai C, Kosulwat V, Mahachoklertwattana P, Rojroongwasinkul N. Elevated serum cholesterol levels in Bangkok children and adolescents. J Med Assoc Thai 1999; 82: S117–S121.
27. Tienboon P, Fuchs G, Linpisarn S, Yutrabootr Y, Nimsakul S, Likit-ekaraj V, Promtet N, Loakuldilok J, Suwankiti S, Suskind R. Obesity and coronary risk factors in Chiang Mai children. Chiang Mai Med Bull 1996; 35: 102.
28. Webber LS, Srinivasan SR, Frerichs RR, Berenson GS. Serum lipids and lipoproteins in the first year of life – the Bogalusa Heart Study. 18th Annual Conference on Cardiovascular Disease. Epidemiol Newslet 1978; p 32.
29. Lauer RM, Lee J, Clarke WR. Factors affecting the relationship between childhood and adulthood cholesterol levels: The Muscatine Study. Pediatrics 1988; 82: 309–318.
30. Jarvelin MR. Congenital heart disease: fetal and infant markers of adult heart diseases. Heart 2000; 84: 219–226.
31. Lucas A. Programming by early nutrition: an experimental approach. J Nutr 1998; 128: S401–S406.
32. Barker DPJ. Fetal nutrition and cardiovascular disease in adult life. Lancet 1993; 341: 938–941.
33. Tienboon P, Rutishauser IHE, Wahlqvist ML. Early life factor affecting body mass index and waist-hip ratio in adolescence. Asia Pac J Clin Nutr 1992; 1: 21–26.
34. Tienboon P. Nutrition concerns during adolescence: precursors for later diseases. J Intern Med India 1999; 2: 188–197.