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LIPIDS AND LIPOPROTEINS IN THE SEXUAL MATURATION STAGES OF MALE ADOLESCENTS*

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SUMMARY: Büyükgebiz A, Ciliv G, Kınık E. (Departments of Pediatrics and Biochemistry, Hacettepe University Faculty of Medicine, Ankara, Turkey). Lipids and lipoproteins in the sexual maturation stages of male adolescents. Turk J Pediatr 33: 19-25, 1991.

The study population consisted of 144 healthy, non-obese male adolescents, aged between 11-18 years, who were in different stages of sexual maturation as described by Tanner. The fasting plasma cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (C-HDL), low density lipoprotein cholesterol (C-LDL), and very low density lipoprotein cholesterol (C-VLDL) levels were calculated for each subject.

There were significant differences observed in the following: mean TC levels between G1 and G2; mean C-HDL levels between G2 and G3 and between G3 and G4; mean TG levels between G1 and G2 and between G2 and G3; mean C-LDL levels between G1 and G2, and mean C-VLDL levels between G1 and G2 and between G2 and G3. There were no significant differences for lipids and lipoproteins between the prepubertal (G1) and postpubertal (G5) stages.

It is generally believed that testosterone may play a role in mediating lipid and lipoprotein levels in the pubertal phase, but, since we found no significant differences in the levels of lipids and lipoproteins between G1 and G5, and also because these levels fluctuated from G1 to G5, it strongly suggests that the effect of testosterone on lipids and lipoproteins is dependent on other factors such as hormones, dietary habits, age, race, etc. *Key words: lipids, lipoproteins, male adolescents, Tanner sexual maturation stages.*

The association of total serum cholesterol (TC) and low density lipoprotein cholesterol (C-LDL) levels with the development of atherosclerosis has been well established[1-3]. However, the high density lipoprotein cholesterol (C-HDL) concentration is inversely related to the incidence of coronory artery disease[4-5].

Age and gender have been demonstrated to affect the C-HDL level[6]. Women tend to have higher C-HDL levels than men. Plasma C-HDL level are similar in both sexes during childhood and adolescence, and by the end of sexual maturation, changes in lipids and lipoproteins occur, which result in "adult" male-female lipoprotein differences[7].

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Most, but not all, cross-sectional and longitudinal studies have reported reductions in plasma cholesterol during adolescence[7-10]. The fall in total plasma cholesterol in males during adolescence is thought to be primarily accounted for by reductions in C-HDL and increases in C-LDL in late adolescence[7]. Subsequently, males maintain lower C-HDL levels than females throughout adult life.

This study was designed to assess cross-sectional changes in lipids, lipoproteins and stages of sexual maturation in male adolescents.

Material and Methods

The study population consisted of one hundred and forty-four healthy, non-obese male adolescents, aged between 11-18 years. The genitalia of each adolescent were classified, by the same observer, according to the stages of development described by Tanner[11], which are as follows: (G1) Prepubertal stage (G2) marked by enlargement of the scrotum and testes and reddening of the scrotal skin. (G3) Further growth of the scrotum and testes and an increase in the size of the penis, mainly in length. (G4) Still further growth of the scrotum and testes and an increase in the size of the penis, mainly in breadth. (G5) Adult developmental stage. Fasting plasma cholesterol, triglyceride (TG), C-LDL, C-HDL and very low density lipoprotein cholesterol (C-VLDL) levels were calculated for each adolescent.

TC was determined by the iron chloride-sulphuric acid method and the C-HDL level by the phosphotungstate-magnesium chloride precipitation technique[12-14]. The TG level was measured colorimetrically[15]. C-LDL and C-VLDL levels were calculated using the following formula: C-LDL (mg/dl):TC-(C-HDL + TG/5); the TG/5 value corresponds to the C-VLDL value[16].

Results

Table I gives a cross-sectional distribution of lipids and lipoproteins according to the Tanner stages of sexual maturation.

There were statistically significant differences observed in the following: mean TC levels between G1 and G2 ($p < 0.05$); mean C-HDL levels between G2 and G3 ($p < 0.001$) and between G3 and G4 ($p < 0.05$); mean TG levels between G1 and G2 ($p < 0.001$) and between G2 and G3 ($p < 0.001$); mean C-LDL levels between G1 and G2 ($p < 0.001$), and mean C-VLDL levels between G1 and G2 ($p < 0.001$) and between G2 and G3 ($p < 0.001$). There were no other statistically significant differences noted between the other stages of Tanner's sexual maturation classification as regards lipids and lipoproteins ($p > 0.05$). In addition, there were no statistically significant differences found in the values for lipids and lipoproteins when comparing the prepubertal (G1) stage with the postpubertal (G5) stage ($p > 0.05$) (Fig. 1).

TABLE I: Distribution of Serum Lipids* and Lipoproteins* According to the Tanner Stages of Genital Development (mean±SD)

Genital Stage	Mean chronological age and range (Yrs)	Number of Adolescents	TC	C-HDL	TG	C-LDL	C-VLDL
G 1	11.3 (11.0–12.2)	26	141.5±27.3	48.6±13.0	100.6±50.4	72.7±22.9	20.2±10.2
G 2	12.0 (11.2–13.4)	25	155.4±11.9	53.0±7.7	48.0±23.6	92.8±17.1	9.6±4.7
G 3	12.9 (11.8–15.1)	30	146.3±29.8	42.9±8.0	105.5±61.5	82.1±28.7	21.2±12.5
G 4	13.8 (12.4–16.4)	32	139.0±15.1	48.4±10.9	82.0±53.5	71.0±10.7	19.5±12.5
G 5	16.2 (14.8–18.0)	31	141.1±25.8	51.4±12.4	110.2±62.0	68.0±27.7	22.0±12.3
			G1vsG2 $p < 0.05$	G1vsG2 $p > 0.05$	G1vsG2 $p < 0.001$	G1vsG2 $p < 0.001$	G1vsG2 $p < 0.001$
			G2vsG3 $p > 0.05$	G2vsG3 $p < 0.001$	G2vsG3 $p < 0.001$	G2vsG3 $p > 0.05$	G2vsG3 $p < 0.001$
			G3vsG4 $p > 0.05$	G3vsG4 $p < 0.05$	G3vsG4 $p > 0.05$	G3vsG4 $p > 0.05$	G3vsG4 $p > 0.05$
			G4vsG5 $p > 0.05$	G4vsG5 $p > 0.05$	G4vsG5 $p > 0.05$	G4vsG5 $p > 0.05$	G4vsG5 $p > 0.05$
			G1vsG5 $p > 0.05$	G1vsG5 $p > 0.05$	G1vsG5 $p > 0.05$	G1vsG5 $p > 0.05$	G1vsG5 $p > 0.05$

* mg/dl

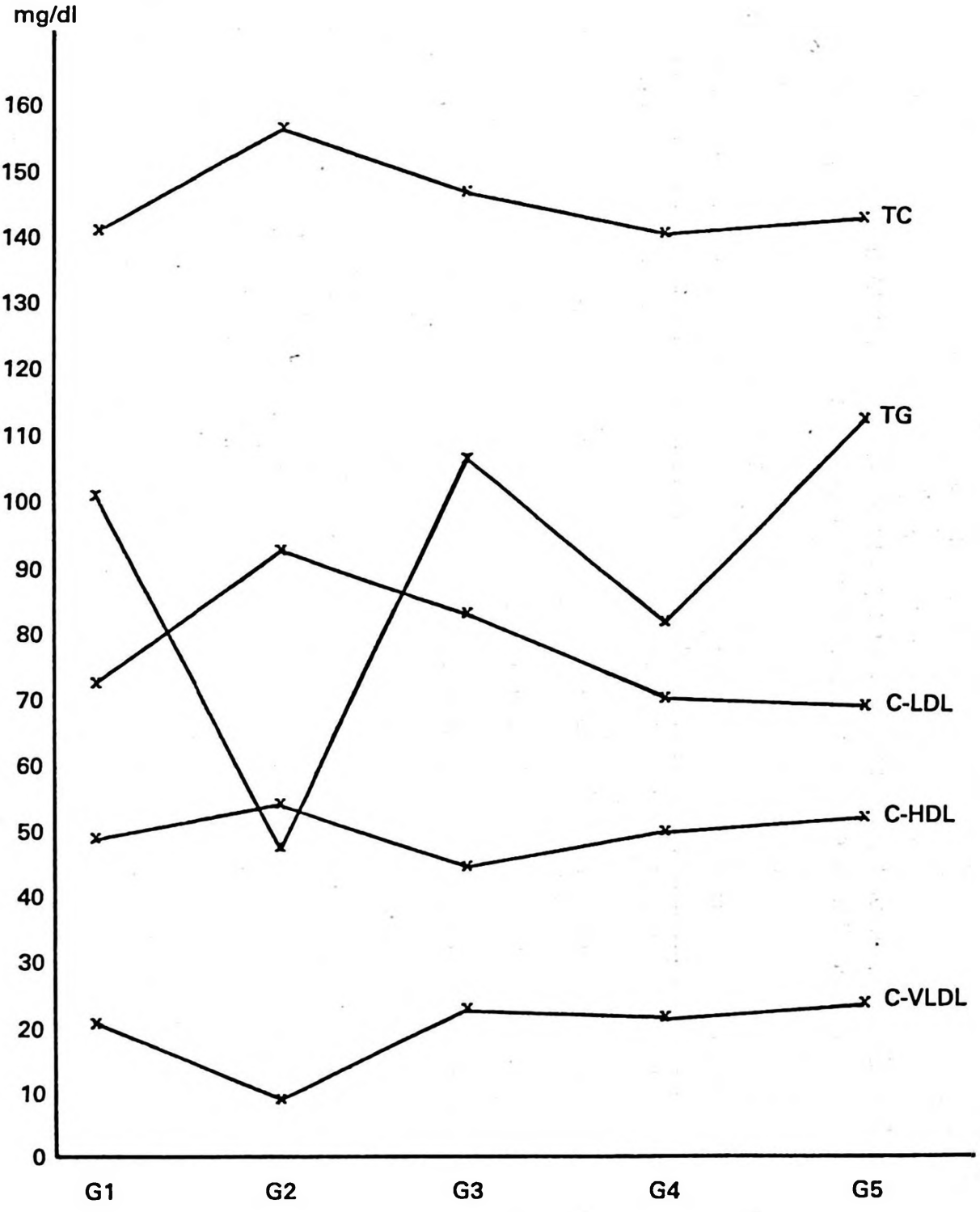

Fig. 1: Mean total cholesterol (TC), tryglyceride (TG), low density lipoprotein cholesterol (C-LDL), high density lipoprotein cholesterol (C-HDL) and very low density lipoprotein cholesterol (C-VLDL) in male adolescents at different Tanner stages.

Discussion

Adolescence is characterized by rapid alterations in physical growth and sexual maturation with a broad distribution of sexual maturation by calendar age[11-17]. Although adolescents follow the same sequence of changes (unless there is an intervening physical or hormonal abnormality), they enter, pass through and complete puberty at different ages.

Appreciable hormonal changes, primarily increased testosterone production in males, accompany the manifestations of adolescence[18-20]. Since the stage of sexual maturation (Tanner Classification), and not the age, coincides with an increase in the testosterone level, the adolescents in our study were classified according to the sexual stages described by Tanner[11,21,22].

Morrison et al[21] speculated that a decrease in C-HDL and a late increase in C-LDL, as sexual maturation progresses, are associated with increased testosterone production. In two studies, one by Barr[23], and the other by Nikkila[24], it was demonstrated that the administration of methyltestosterone in adult males produced a decrease in C-HDL and an increase in C-LDL. However, in 1987, Kirkland et al[22] reported just the contrary, as regards the relationship of testosterone to -HDL, and emphasized that testosterone should be considered a significant determinant of plasma C-HDL levels during pubertal development. Although in our study there was a decline in C-HDL levels in the G3, G4 and G5 stages with respect to G2, those values were statistically insignificant. We found a sharp increase in C-LDL in the early pubertal stage (G2), and not in the late pubertal stages, as Morrison had mentioned[21]. Even though it is known that in adolescence plasma testosterone increases, the values of C-HDL and G-LDL in the various Tanner Stages might be the result of the effects of testosterone on these two lipoproteins. Although Bradley[25] mentioned that an inverse relationship exists between TG and C-HDL, the increase in TG during sexual maturation which accompanies the decrease in C-HDL is expected. Since we obtained significantly higher TG levels in G3 with respect to G2, the high levels in G3, G4 and G5 were not significantly different from each other.

Since there is a relationship between C-VLDL and TG, we found a significant decline in G2 with respect to G1, and a significant increment in G3 with respect to G2, which are similar to TG results. Whether the initiating step in the sequential changes in C-HDL and TG during sexual maturation in males is a testosterone-mediated effect on high density lipoproteins, with a secondary reduction in C-VLDL removal or vice versa, remains to be determined by kinetic studies[23-25].

In conclusion, we believe that testosterone may play a role in mediating the levels of lipoproteins and lipids in the pubertal phase but the presence of statistically insignificant differences between prepubertal (G1) and postpubertal (G5) lipid and

lipoprotein levels and the fact that these levels fluctuate in the pubertal stages from G1 to G5, support the view that the effect of testosterone on lipids and lipoproteins is mediated by a combination of other factors (hormones, dietary, habits, age, race, etc) during puberty.

REFERENCES

1. Kannel WB, Castelli WP, Gordon T, et al. Serum cholesterol, lipoproteins and the risk of coronary heart disease: The Framingham study. *Ann Intern Med* 74:1, 1971.
2. Castelli WP, Doyle JT, Gordon T, et al. HDL cholesterol and other lipids in coronary heart disease: The cooperative lipoprotein phenotyping study. *Circulation* 55:767, 1977.
3. Carlson LA, Böttiger LE. Ischaemic heart-disease in relation to fasting values of plasma triglycerides and cholesterol. Stockholm prospective study. *Lancet* 1:865, 1972.
4. Miller GJ, Miller NE. Plasma-high-density-lipoprotein concentration and development of ischamic heart-disease. *Lancet* 1:16, 1975.
5. Miller NE, Thelle DS, Forde OH, et al. The Tromsø heart-study high-density lipoprotein and coronary heart-disease: a prospective case-control study. *Lancet* 1:965, 1977.
6. Rifkind BM, Tamir I, Heiss G, et al. Distribution of high density and other lipoproteins in selected LRC prevalence study populations: a brief survey. *Lipids* 14:105, 1979.
7. Morrison JA, deGroot I, Edwards BK, et al. Lipids and lipoproteins in 927 schoolchildren, ages 6 to 17 years. *Pediatrics* 62:990, 1978.
8. Lauer RM, Connor WE, Leaverton PE, et al. Coronary heart disease risk factors in school children: Muscatine study. *J Pediatr* 86:697, 1975.
9. Frerichs RR, Srinivasan SR, Webber LS, et al. Serum cholesterol and triglyceride levels in 3,446 children from a biracial community: the Bogalusa Heart Study. *Circulation* 54:302, 1976.
10. Morrison JA, deGroot I, Edwards BK, et al. Plasma cholesterol and triglyceride levels in 6,775 school children, ages 6-17. *Metabolism* 26:1199, 1977.
11. Marshall WA, Tanner JM. Variations in the pattern of pubertal changes in boys. *Arch Dis Child* 45:13, 1970.
12. Leffler HH, McDougald CH. Estimation of cholesterol in serum by means of improved technics. *Techn Bull Regist Med Techn* 33:19, 1963.
13. Burstein M, Scholnick HR, Morfin R. Rapid method for the isolation of lipoproteins from human serum by precipitation with polyanions. *J Lipid Res* 11:583, 1970.
14. Lopes-Virella MF, Stone P, Ellis S, et al. Cholesterol determination in high-density lipoproteins separated by three different methods. *Clin Chem* 23:882, 1977.
15. Sigma Technical Bulletin No: 405. The quantitative colorimetric determination of triglycerides in serum or plasma. Sigma Chem. Co. St. Louis, Missouri, 63178.
16. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* 18:499, 1972.
17. Marshall WA, Tanner JM. Variations in the pattern of pubertal changes in girls. *Arch Dis Child* 44:291, 1969.
18. Gupta D, Attanasio A, Raaf S. Plasma estrogen and androgen concentrations in children during adolescence. *J Clin Endocrinol Metab* 40:636, 1975.

19. August GP, Grumbach MM, Kaplan SL. Hormonal changes in puberty, 3. Correlation of plasma testosterone, LH, FSH, testicular size, and bone age with male pubertal development. *J Clin Endocrinol Metab* 34:319, 1972.

20. Baker HW, Burger HG, Kretser DM, et al. Changes in the pituitary-testicular system with age. *Clin Endocrinol* 5:349, 1976.

21. Morrison JA, Laskarzewski P, Rauh JL, et al. Lipids, lipoproteins, and sexual maturation during adolescence: the Princeton maturation study. *Metabolism* 28:641, 1979.

22. Kirkland RT, Keenan BS, Probstfield JL, et al. Decrease in plasma high-density lipoprotein cholesterol levels at puberty in boys with delayed adolescence. Correlation with plasma testosterone. *JAMA* 257:502, 1987.

23. Barr DP, George E. Brown memorial lecture; some chemical factors in pathogenesis of atherosclerosis. *Circulation* 8:641, 1953.

24. Nikkila EA. metabolic regulation of plasma high density lipoprotein concentrations [editorial]. *Eur J Clin Invest* 8:111, 1978.

25. Bradley DD, Wingerd J, Petitti DB, et al. Serum high-density-lipoprotein cholesterol in women using oral contraceptives, estrogens and progestins. *N Engl J Med* 299:17, 1978.