Lipid Profile of Cord Blood in Term Newborns

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Background: Hyperlipidemia is an important risk factor for coronary artery disease. Detection of lipid profile in umbilical cord blood of term newborns could identify neonates with a higher risk of coronary artery disease.

Objectives: The aim of the present study was to improve the existing information about cord blood lipid profile of Iranian term newborns.

Patients and Methods: This cross-sectional study was conducted on healthy term neonates born from healthy mothers between August and October 2009 in Zanjan, Iran. Ten milliliters of cord blood was collected from the placental end of umbilical vein immediately after the cord clamping. Total cholesterol (TC) and triglyceride (TG) were measured by enzymatic GOD-PAP method with Pars Azmoon kits. High-density lipoprotein-cholesterol (HDL-C) was measured after precipitation of Apo lipoproteins with phosphotungstic acid (PTA). Low-density lipoprotein-cholesterol (LDL-C) was calculated by Friedewald’s formula. Statistical Analysis was performed by the SPSS statistical package version 16.0 for windows.

Results: Of the 174 neonates, 97 were female. Vaginal delivery was recorded in 79.8%. There were no significant differences regarding demographic findings between male and female neonates. The mean values of TC, LDL-C, HDL-C and TG were 73.1 ± 26.5, 28.7 ± 11.1, 27.6 ± 10, and 81.4 ± 37.1mg/dL respectively, with no difference between the two sexes.

Conclusions: We found a relatively high value of TC and TG in our study. Considering the relationship between high levels of lipids in the neonatal period and coronary artery disease in the adult population, we recommend future cohort studies for this statistical society.

Keywords: Cord Blood; Lipid; Newborn Infants

1. Background

Coronary artery disease (CAD) is an important leading cause of mortality in the world (1, 2). The prevalence of CAD related mortality has increased (3, 4); this increase was more dramatic in developing countries with the age of onset of disease being reduced during the recent years (5-7). The process of this disease begins early in life and gradually progresses throughout the following years (8). Hyperlipidemia is an important risk factor for cardiovascular disease (9). A strong independent relationship between childhood and adulthood serum lipids has been reported (10). There are evidences of such associations originating at birth (10-12). There are many reports of hyperlipidemia at young ages (13-15), in recent years there are some reports of high cord blood triglyceride level from Iran (16-19). The high triglyceride level may be due to the relatively high frequency of vitamin D deficiency in Iranian newborns (20). Some reports have indicated that the serum level of vitamin D has an inverse relationship with blood triglyceride level (21, 22). Prevention of CAD must be initiated at younger ages, because there is an opportunity to begin preventive interventions for cardio-vascular risk factors (23), furthermore the study of CAD risk factors is greatly recommended during this period. There are many researches about cord blood lipid profiles in the literature with some controversies (24-36). Detection of these markers in umbilical cord blood of term newborns could identify neonates at higher risk of coronary heart disease (29, 30).

2. Objectives

The aim of this study was to gather more information for analyzing the cord blood lipid profile of term newborn infants and compare the findings with other reports.

3. Patients and Methods

This cross-sectional study was conducted from August to October 2009 in Zanjan city at a public general hospital affiliated with Zanjan University of Medical Sciences, Iran (Zanjan is located in the northwest of Iran). This research was approved by the ethical committee and financially supported by the deputy of research of Zanjan University of Medical Sciences. The aim of the study was explained to all the candidate’s mothers before obtaining a written informed consent. The study group was selected from healthy term neonates born to healthy mothers with no history of diabetes, eclampsia and preeclampsia,
dyslipidemia and other chronic diseases. Neonates with gestational age of less than 37 weeks, congenital anomaly, five minute Apgar score of less than seven, and sick newborns were excluded. Gestational age was recorded based on the last menstruation date and sonographic information. The weight, height and head circumference of the neonates were measured with standard methods and body mass index (BMI) was calculated immediately after delivery. Ten milliliters of cord blood was collected from the placental end of the umbilical vein immediately after cord clamping. Serum was separated by centrifugation and frozen at -70°C. All samples were analyzed for lipid profiles including total cholesterol (TC), triglyceride (TG) and high-density lipoprotein-cholesterol (HDL-C). An auto analyzer (Selectra II, Netherland) was used to determine the lipid profiles. Total cholesterol and TG were measured by GOD PAP enzymatic method using cholesterosterase, cholesterol oxidase and glycerol phosphate oxidase test with Pars Azmoon kits with a sensitivity of 0.5 mg/dL. High-density lipoprotein-cholesterol was measured after precipitation of Apo lipoproteins with phosphotungstic acid (PTA). Low-density lipoprotein-cholesterol was calculated by Friedewald’s formula (31). A lipid standard (CFAS/Boehringer Mannheim, cat. no. 759350) was used to calibrate the selectra 2 auto analyzer. Assay performance was checked after every 20 tests using the lipid control serum perineum (normal range) and percipat (pathologic range), wherever applicable. Inter- and intra-coefficients of variation (CV) for the assay (TC or TG) were 1.1% and 1.6% for the lower limit, 0.9% and 0.6% for the upper limit, respectively (calculated in mg/dL). Statistical Analysis was performed using the SPSS software version 16.0. Continuous data were expressed as mean ± standard deviation (SD). The Student’s t-test and Mann-Whitney test were applied for comparison of mean values wherever appropriate. The relationship between cord blood lipid profile and quantities of birth weight and gestational age was determined by the Mann Whitney regression test. Spearman correlation coefficient was used to find a correlation between these variables. The significance level was set at P value < 0.05.

4. Results

One-hundred and seventy-four neonates including 97 females and 77 males were included in this study. Vaginal delivery was recorded in 139 (79.8%) and unwanted pregnancies in 27 (15.5%) of the subjects; maternal ages were between 14 and 40 years. All newborns were term and near term. Their weight ranged from 2500 to 3970 grams. Height and head circumference were 45-56 cm and 31-37 cm, respectively. Body mass index was calculated as 10.3-16.1. Demographic findings of the study population are demonstrated in Table 1. There were no significant differences regarding demographic findings between male and female neonates. There was no difference between vaginal delivery and cesarean sections regarding cord blood lipids. Minimum, maximum and total mean level of lipid concentrations in this study have been shown in Table 2. There was no difference between the two sexes regarding the mean value of TC, TG, HDL-C and LDL-C. A significant positive correlation was observed between cord blood TC and TG (r = 0.42, P < 0.01), as well as between TG and non HDL-C (r = 0.39, P <0.01), TG and HDL-C (r = 0.23, P < 0.01) and TG and LDL level (r = 0.22, P < 0.01). No significant correlations were detected between lipid concentrations and demographic finding of neonates, yet there was a negative significant correlation between cord blood TG concentration and maternal age (r = -0.15, P = 0.03).

| Variable                  | Total (No. =174) | Male (No. =77) | Female (No. =97) | P Value |
|---------------------------|------------------|----------------|------------------|---------|
| Gestational Age, Week     | 39.1 ± 0.9       |                |                  |         |
| Maternal Age, y           | 26.3 ± 5.9       |                |                  |         |
| Neonatal Weight, gr       | 3166 ± 32.9      | 3218 ± 292     | 3124 ± 352       | 0.063   |
| Height, cm                | 50.1 ± 1.8       | 50.3 ± 1.7     | 49.9 ± 1.9       | 0.19    |
| Head Circumference, cm    | 33.9 ± 1.4       | 34.1 ± 1.4     | 33.8 ± 1.3       | 0.23    |
| BMI, kg/m²                | 12.6 ± 1.1       | 12.7 ± 1       | 12.5 ± 1.2       | 0.26    |

Data are presented as Mean ± SD.

| Variables, Level of Lipid | Minimum | Maximum | Total, Mean ± SD |
|---------------------------|---------|---------|------------------|
| TC, mg/dL                 | 39      | 229     | 73.1 ± 26.5      |
| TG, mg/dL                 | 31      | 270     | 81.4 ± 37.1      |
| HDL-C, mg/dL              | 11      | 78      | 27.6 ± 10        |
| LDL-C, mg/dL              | 15      | 100     | 28.7 ± 11.1      |

Abbreviations: TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

5. Discussion

There are different reports of cord blood lipid values from various geographical areas (Table 3). In this study we wanted to compare the level of cord blood lipids in our normal term infants of healthy mothers with other articles. In the present study the mean value of TC, LDL-C, HDL-C and TG were 73.1 ± 26.5, 28.7 ± 11.1, 27.6 ± 10, and 81.4 ± 37.1mg/dL, respectively. These findings are similar to some other studies from Iran (Table 3) yet different from the values reported from certain countries, and this can be related to conditions that affect fetal growth, such as ethnicity and diet.
In comparison to studies conducted in other countries, the mean value of TC in our study was similar to the findings of Kharb et al. with 100 healthy newborn samples in India (27), lower than the report of Juarez et al. with 200 newborns in Mexico (36), and higher than the findings of Mahley et al. with 105 Turkish newborns (32) and Casanuv et al. from Chile with 156 normal newborns (30). Our TC level was lower than studies from other parts of Iran like the study of Badiee et al. from Isfahan (17) and Vaziri Esfarjani et al. from Ahvaz (37), yet higher than the study of Ghiasi et al. from Tehran (33). In the present study the level of LDL-C was lower than studies from Mexico (36), Chile (30) and India (27) and higher than the study from Turkey (32). Compared to other studies from Iran, the level of LDL-C in our study was lower than the study of Badiee et al. from Isfahan (17) and Vaziri Esfarjani et al. from Ahvaz (37), yet higher than the study of Ghiasi et al. from Tehran (33). The level of HDL-C in our study was similar to that reported by a study from Chile (30) and lower than studies from Mexico (36) and Turkey (32) and higher than a study from India (27). In this study, the mean value of TG in 33% of females and 35% of males was higher than the 95th percentile of triglyceride level reported in the Nelson textbook of Pediatrics, which indicates a high frequency of cord blood hypertriglyceridemia in our subjects (34). There are other reports of high cord blood hypertriglyceridemia in Iran (16, 17, 19, 37), yet the level of cord blood TG in our study was higher than other reports from Iran (17, 33). High triglyceride level may be due to the relatively high frequency of vitamin D deficiency in Iranian newborns (20, 21). In our study there were no significant differences between the two sexes regarding the mean value of TC, LDL-C, HDL-C and TG, which is different from the results of some previous studies (17, 27, 37) and similar to the reports of Ghiasi et al. (33). There was no statistically significant association between lipid levels and anthropometric parameters in our study. In the study of Ghiasi et al. in Tehran (33), there was no statistically significant association between lipid levels and anthropometric parameters in males but there was a significant inverse correlation between TG level and head circumference in female newborns (33). In the present study, there was no difference between vaginal delivery and cesarean section regarding cord blood lipids. In the study of Yoshimitsu N et al. in Japan, TC and non-HDL levels in cord blood showed a correlation with maternal and fetal lipid levels. A correlation coefficient (> 0.3) was noted in the caesarean section group (35). The first limitation of this study was the lack of mother’s serum lipid levels in the data, and the second limitation was the study’s cross sectional design. In future studies, by checking the mother’s lipid and using longitudinal data, additional valuable information can be provided. We found a relatively high level of TC and TG in our study. Considering the relationship between high levels of lipids in the neonatal period and cardiovascular diseases in the adult population, we recommend future cohort studies to further unveil the involved mechanisms.

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Authors’ Contributions
Seyed Alinaghi Kazemi and Mansur Sadeghzadeh prepared the manuscript, designed the project, collected, analyzed and interpreted the data.

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References
1. Pardo IM, Geloneze B, Tambascia MA, Barros-Filho AA. Atherosgenic lipid profile of Brazilian near-term newborns. Braz J Med Biol Res. 2005;38(5):755-60.
2. Nichols M, Townsend N, Scarborough P, Rayner M. Trends in age-specific coronary heart disease mortality in the European Union over three decades: 1980-2009, Eur Heart J. 2013;34(39):3017-27.
3. Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases: part 1: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. Circulation. 2001;104(22):2746-53.
4. Gaziano TA, Bitton A, Anand S, Abrahams-Gessel S, Murphy A. Growing epidemic of coronary heart disease in low- and middle-income countries. Curr Prob Cardiol. 2010;35(2):72-115.
5. Thornburg K L. Fetal origin of cardiovascular disease. Am Acad Cardiov Dis. 2004;5:527-34.
6. Reddy KS. Cardiovascular diseases in the developing countries: dimensions, determinants, dynamics and directions for public health action. Public Health Nutr. 2002;5A(1A):221-7.
7. Jafari N, Abbolahessani F, Naghabi M, Pourmalek F, MoradiLakeh M, Kazemeini H, et al. National burden of disease and study in Iran. Iran J Public Health. 2009;38(Suppl 1):7-3.
8. Hong YM. Atherosclerotic cardiovascular disease beginning in
childhood. *Korean Cir*. 2010;40(1):3–9.

9. Banerjee R, Bhattacharjee S, Ray K, KumarRoy J, Datta S, Banerjee I. Dyslipidemia and its Relationship with Cardiovascular Risk Factors in a Selected Population of Siliguri City, West Bengal, India. *Asian J Med Sci*. 2011;5(3).

10. Magon P, Bharatwaj RS, Verma M, Chatwal J. Cord Blood Lipid Profile at Birth Among Normal Indian Newborns and Its Relation to Gestational Maturity and Birth Weight: A Cross Sectional Study. *Indian J Res*. 2013;7(2):215–8.

11. Bastida S, Sanchez-Muniz FJ, Cuena R, Perea S, Aragones A. High density lipoprotein-cholesterol changes in children with high cholesterol levels at birth. *Eur J Pediatr*. 2002;160(2):94–8.

12. Nayak CD, Agarwal V, Nayak DM. Correlation of Cord Blood Lipid Heterogeneity in Neonates with Their Anthropometry at Birth. *Indian J Clin Biochem*. 2012;28(2):352–7.

13. Azizi F, Aazadbakt I, Mirrinnan P. Trends in overweight, obesity and central fat accumulation among Tehranian adults between 1998-1999 and 2001-2002: Tehran lipid and glucose study. *Ann Nutr Metab*. 2005;49(1):1–8.

14. Kelishadi R, Hashemipour M, Sarraf-Zadegan N, Amiri M. Trend of Atherosclerosis Risk Factors in Children of Isfahan. *Asian Cardiovasc Thorac Ann*. 2001;9(1):36–40.

15. Kelishadi R, Pour MH, Zadegan NS, Kahlbazi M, Sadry G, Amani A, et al. Dietary fat intake and lipid profiles of Iranian adolescents: Isfahan Healthy Heart Program–Heart Health Promotion from Childhood. *Prev Med*. 2004;39(4):760–6.

16. Kazemi SA, Mousavinasab N, Mellati AA, Sadeghzadeh M. A report of high triglyceride level in cord blood of Iranian newborns. *Int J Prev Med*. 2013;4(7):755–6.

17. Badiee Z, Kelishadi R. Cord blood lipid profile in a population of Iranian term newborns. *Pediatr Cardiol*. 2008;29(3):574–9.

18. Vaziri Esfarjani S, Iravani E, RazaghiAzar M. Determination of the Lipid Profile of Cord Blood in Neonates and its Correlation with Maternal Age in Iran. *J Compr Pediatr*. 2012;2(2).

19. Mellati AA, Mazloomzadeh S, Anjomshoaa A, Alipour M, Karimi F, Mazloomi S, et al. Multiple correlations between cord blood lipoprotein, apolipoprotein levels. *Indian J Res*. 2012;4(1):35–8.

20. Kazemi A, Sharifi F, Jafari N, Mousavinasab N. High prevalence of vitamin D deficiency among pregnant women and their newborns in an Iranian population. *J Womens Health (Larchmt)*. 2009;18(6):835–9.

21. Reijnmark L, Vestergaard P, Heickendorff L, Mosekilde L. Simvastatin does not affect vitamin d status, but low vitamin d levels are associated with dyslipidemia: results from a randomised, controlled trial. *Int J Endocrinol*. 2010;2010:957874.

22. Mok CC, Birmingham DJ, Leung HW, Hebert LA, Song H, Rovin BH. Vitamin D levels in Chinese patients with systemic lupus erythematosus: relationship with disease activity, vascular risk factors and atherosclerosis. *Rheumatology (Oxford)*. 2012;51(4):644–52.

23. Kelishadi R, Pashmi R, Sarraf-Zadegan N, Ahmadi MM, Mohammadm Zadeh M, Pashmi R. Healthy heart program: heart health promotion from childhood. *J Qazvin Univ Med Sci*. 2003;26(9):25–26.

24. Xiao-yun C. A study of changes of leptin, cholesterol and triglyceride in cord blood of newborns. *J Transl Med Coll*. 2008;30.

25. Bansal N, Cruickshank JK, McElfu P, Durrington PN. Cord blood lipoproteins and prenatal influences. *Curr Opin Lipidol*. 2005;16(4):400–8.

26. Kharr S, Kaur A, Nanda S. Comparison of cord blood atherogenic index in males and females. *Cardiovasc Rev*. 2009;4(1):35–8.

27. Kharr S, Singh V, Sangwan K. Correlation of birth weight and cord blood lipoprotein, apolipoprotein levels. *Adv Med Dent Sci*. 2009;3(4):13–6.

28. Kelishadi R, Badiee Z, Adeli K. Cord blood lipid profile and associated factors: baseline data of a birth cohort study. *Puediatr Peri- nat Epidemiol*. 2007;21(5):318–24.

29. Srinivasan SR, Berenson GS. Serum apolipoproteins A1 and B as markers of coronary artery disease risk in early life: the Bogalusa Heart Study *Clin Chem*. 1995;41(1):159–64.

30. Casanueva V, Cid X, Chiang MT, Molina M, Ferrada MC, Perez R, et al. [Lipids, lipoproteins and apolipoproteins in normal newborns]. *Rev Med Chil*. 1998;126(9):1073–8.

31. 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*. 1972;18(6):499–502.

32. Mahley RW, Arslan P, Pekcan G, Pepin GM, Agacikten A, Karago- glu N, et al. Plasma lipids in Turkish children: impact of puberty, socioeconomic status, and nutrition on plasma cholesterol and HDL. *J Lipid Res*. 2008;49(2):1996–2006.

33. Ghiassi A, Ziaee S, Faghihizadeh S. A Comparison of Lipid and Lipoprotein B-100 (Apo B-100) Levels in the Umbilical Cord Blood of Male and Female Newborns and the Assessment of their impact on Neonatal Anthropometric Indices. *Modares J Med Sci Pathobiol*. 2013;16(4):55–62.

34. Neal W. Disorders of lipoprotein Metabolism and Transport. In: Behrmann RE, Kligman RM, Arvin AM editors. *Nelson textbook of pediatrics*. 18th ed. Philadelphia: W. B. Saunders Co; 2007. pp. 580–93.

35. Nagasaki H, Chiba H, Kikuta H, Akita H, Takahashi Y, Yanai H, et al. Unique character and metabolism of high density lipoprotein (HDL) in fetus. *Atherosclerosis*. 2002;161(2):219–23.

36. Juarez IE, Rivera-Silva G, Mejia-Arangure JM, Mercado-Arellano JA, Diaz-Bensussen S. [Lipid profile in healthy newborn infants and its correlation with maternal lipid levels]. *Salud Publica Mex*. 1999;41(4):405–9.

37. Vaziri Esfarjani S, Iravani E, RazaghiAzar M. Determination of the Lipid Profile of Cord Blood in Neonates and its Correlation with Maternal Age in Iran. *J Compr Pediatr*. 2012;3(2).