

DETERMINATION OF SERUM LIPOPROTEINS IN BETA-THALASSEMIA TRAIT AND THEIR RELATIONSHIP TO CHRONIC HEMOLYSIS

M. PEDRAM, M.D., MRCP, K.M. ZANDIAN, M.D., B. KEYKHAI, M.D., S.A.H. JAHANMEHR, Ph.D., AND M.R. MOHEGH,* M.Sc.

*From the Department of Hematology and Oncology, Shafa Hospital, Ahwaz University of Medical Sciences, and *Dept. of Laboratory Sciences, Ahwaz, Islamic Republic of Iran.*

ABSTRACT

100 patients with beta-thalassemia trait, comprised of 55 men and 45 women, participated in a study to measure serum lipoproteins. The results were compared with the data obtained from 100 control subjects of the same age and sex. A significantly lower level of mean serum total cholesterol and LDL cholesterol, and a much higher level of HDL cholesterol were obtained in beta-thalassemia trait as compared to control groups. This study was carried out in order to find the effect of mild hemolysis on serum lipid composition.

Keywords: Beta-thalassemia, Serum lipoproteins, Chronic hemolysis.

MJIRI, Vol. 10, No. 4, 263-265, 1997.

INTRODUCTION

Thalassemias are a group of chronic, inherited microcytic anemias characterized by reduced rate of synthesis of one or more of the globin chains, leading to imbalanced globin chain synthesis, defective hemoglobin production, red cell damage and therefore chronic hemolysis.¹ Hemolysis is also seen in sickle cell disease, although its mechanism is different. Mild hemolysis appears to have a protective effect on the development of atherosclerosis. In patients with sickle cell disease, myocardial infarction is an extremely rare event,² compared to cerebrovascular accidents in the other parts of the body, and atherosclerosis is virtually nonexistent.³ This population has normal coronaries, frequently of larger caliber than those seen in normal hearts.⁴ Maioli and coworkers found that total and low density lipoprotein (LDL)-cholesterol levels were significantly lower in beta-thalassemia trait carriers when compared to con-

trols, whereas plasma triglycerides and high density lipoprotein (HDL)-cholesterol levels are similar in the two groups.⁵ They suggested that this phenomenon can be due to accelerated erythropoiesis and increased uptake of LDL by the reticuloendothelial system. In patients with homozygous beta thalassemia, the levels of total LDL and HDL cholesterol were found to be significantly lower than in controls.⁶

However, a Libyan family with three sons, resulting from a consanguineous marriage was described.⁷ They had an unusually high concentration of hemoglobin A₂ and hypercholesterolemia, some of them with widespread xanthomas.

Therefore a hypothesis is now to determine if mild and chronic hemolysis can affect serum lipoprotein levels so that a delay or prevention of ischemic heart disease may occur. This hypothesis is followed here to see whether a particular level of serum lipoproteins controlled by a substantial amount of hemolysis can reduce the risk of atherosclerosis and its unwanted consequences.

Request for reprints: Dr. S.A. Hamid Jahanmehr, Clinical Laboratory, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran.

MATERIALS AND METHODS

Total, HDL and LDL cholesterol were measured by enzymatic precipitation techniques^{8,9} with a Technicon RA-1000 autoanalyzer (Technicon Instruments, USA), using commercially available Randox kits (Randox Laboratories Ltd, UK). Samples were obtained after 12 hours of fasting from 100 patients with beta-thalassemia trait, including 55 males and 45 females. Patients and controls ranged in age from 20 to 40 years old, and patients were chosen from those with mean cell volumes (MCV) below normal and HbA₂ levels above 3.5%. The data was then statistically analyzed using student T-test. Smokers and individuals on contraceptive pills or those with hypertension, diabetes mellitus, hyperlipidemia, hypothyroidism as well as subjects who had undergone a recent surgical operation were excluded from this study.

RESULTS

Mean total cholesterol in patients and the control group is compared in Fig. 1. The comparison for LDL is shown in Fig. 2. The values of serum cholesterol and LDL are significantly less than those of the control group ($p < 0.001$). On the contrary, much higher levels of HDL were obtained ($p < 0.01$ for males and $p < 0.001$ for females) as compared with control subjects (Fig. 3). The ratio of total cholesterol/HDL, the value known as "risk factor" (Fig. 4), and the ratio of LDL/HDL (Fig. 5), are significantly reduced in patients compared to the controls ($p < 0.001$).

DISCUSSION

The influence of accelerated erythropoiesis and red cell damage on the level of serum lipoproteins in patients with beta-thalassemia or sickle cell disease appears to lead to changes in favour of prevention or delay of atherosclerosis and ischemic heart disease.²⁻⁵ In one review of the postmortem literature in sickle cell disease, including examination of 153 hearts, only four infarcts were reported.³ Also, atherosclerosis was seen in none of the one hundred hearts of patients (55 of whom were 16 to 47 years old, with a median age of 30) examined at autopsy.² This is in marked contrast to the Vietnam study, in which atherosclerosis was found in 45 percent of 105 battle casualties.¹¹ The exact cause of this apparently protective effect on atherosclerosis is unknown, but may involve genetic or dietary factors, or anemia itself.¹⁰ This protective effect is probably due to phagocytosis of damaged red cells and increased ingestion of LDL by macrophages and histiocytes, as the main determinants of low plasma cholesterol levels in heterozygous beta-thalassemia.⁵ In this study, patients with heterozygous beta-thalassemia have significantly low levels of total cho-

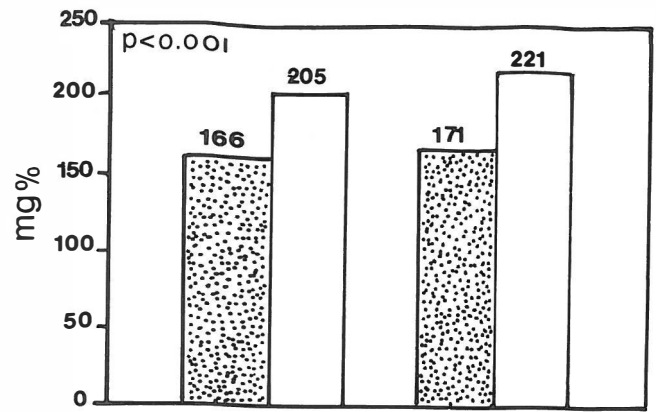


Fig. 1. Mean total cholesterol of patients and controls.

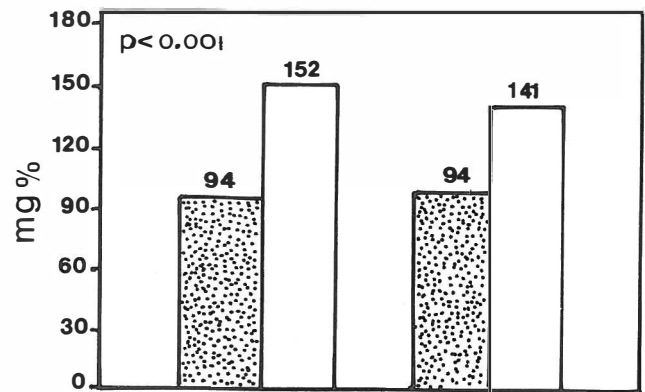


Fig. 2. LDL of patients and control groups.

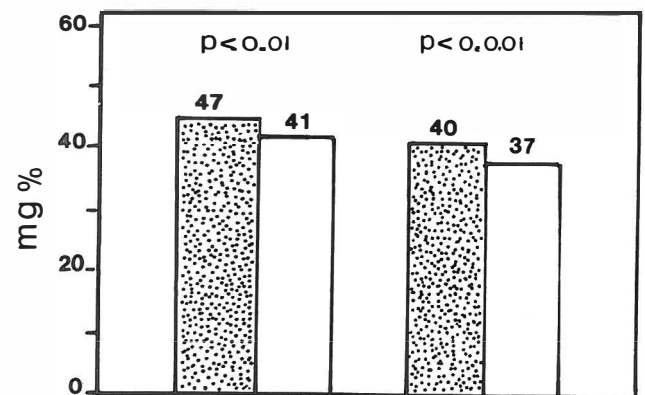


Fig. 3. HDL of patients and controls.

patients controls

lesterol (Fig. 1) and LDL (Fig. 2). The levels of HDL (Fig. 3) in these patients are higher than normal. This situation produces a significant low risk factor for atherosclerosis, as determined by the ratio of total to HDL-cholesterol (Fig. 4). The results obtained from this work confirm the hypothesis that mild and chronic hemolysis, by any means, can have a protective effect to reduce the risk of atherosclerosis, ischemic heart disease and myocardial infarction. Further work is yet to be done in this field of study to understand the mechanism

ACKNOWLEDGEMENT

We are sincerely grateful to Mr. S.M. Latifi, Statistician, Faculty of Hygiene, Ahwaz University of Medical Sciences, Ahwaz, Iran, for kindly analyzing the statistical data.

REFERENCES

1. Weatherall DJ: The Thalassemias. In: Williams JW, Beutler E, Erselev AJ, and Lichtman MA, (eds.), Hematology. 4th edition, New York, McGraw-Hill Publishing Co., pp. 510, 1990.
2. Lindsey J Jr, Meshel JC, et al: The cardiovascular manifestations of sickle cell disease. Arch Intern Med 133: 643, 1974.
3. O'Neill B Jr, Saunders DE Jr, et al: Myocardial infarction in sickle cell anemia. Am J Hematol 16: 139, 1984.
4. Gerry JL, Bulkley BH, et al: Clinicopathologic analysis of cardiac dysfunction in 52 patients with sickle cell anemia. Am J Cardiol 42: 211, 1978.
5. Maioli M, Pettinato S, Cherchi GM, Giraudi D, Pacifico A, Pupita G, Tidore MG: Plasma lipids in beta-thalassemia minor. Atherosclerosis 75: 2, 3, 245-248, 1989.
6. Goldfarb AW, Rachmilewitz EA, Eisenberg S: Abnormal low and high density lipoproteins in homozygous beta-thalassaemia. Brit J Haematol 79(3): 481-486, 1991.
7. Sheriff DS, el-Fakhri EL: The Libyan family with beta-thalassemia trait associated with hypercholesterolemia with widespread xanthomas. Clin Chem 34: 11, 2385-2386, 1988.
8. Segal P, Bachorik PS, Rifkind BM, Levy RI: Lipids and dyslipoproteinemia. In: Henry JB, Davidson TS, (eds.), Clinical Diagnosis and Management by Laboratory Methods. 18th edition, Philadelphia, W.B. Saunders Co., pp. 180-203, 1991.
9. Stein EA, Myers GL: Lipids, Lipoproteins and apoproteins. In: Teitz NW, (ed.), Textbook of Clinical Chemistry. Philadelphia, W.B. Saunders Co., pp. 1002-1093, 1994.
10. Platt OS, Dover GJ: Sickle cell disease. In: Nathan DG, Oski FA, (eds.), Hematology of Infancy and Childhood. 4th edition, Philadelphia, W.B. Saunders Co., pp. 732-782, 1993.
11. McNamara JJ, Molot MA, Jr, et al: Coronary artery in combat casualties in Vietnam. JAMA 216: 1185, 1971.

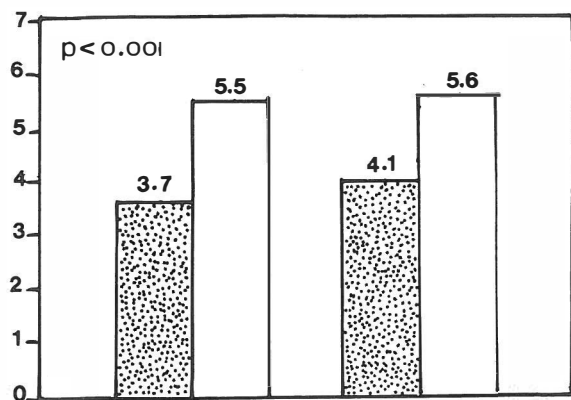


Fig. 4. Ratio of total/HDL cholesterol (risk factor) in patients and controls.

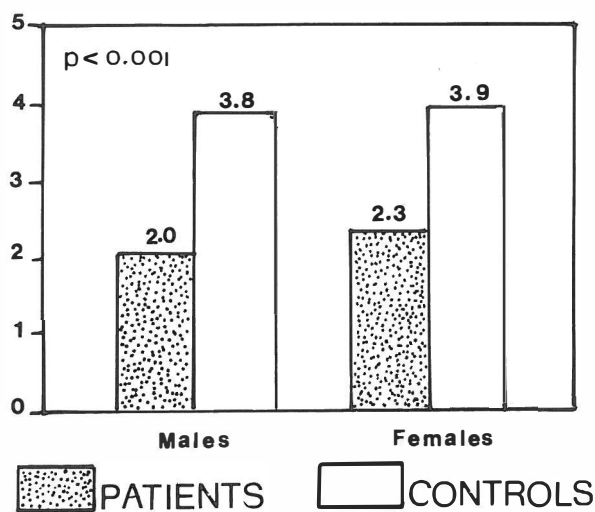


Fig. 5. Ratio of LDL/HDL cholesterol in patients and control groups.

of this protection. The continuation of this work is therefore recommended in cardiac care centers to find the incidence of thalassemia and sickle cell disease in patients suffering from atherosclerosis and heart disease.

