

Regression Analysis of cardiovascular disease risk markers in Nephrotic Syndrome

Bafna Angurbala*¹, Sarkar Purnima Dey², Maheshwari Rameshwar¹, Rangwala Tasneem¹
Batham Anil Rai¹ and Sharma Sandhya¹ Bafna Shashank

¹Department of Biochemistry, Govt. Holkar Science College, Indore, Madhya Pradesh, India

²Department of Biochemistry, MGM Medical College, Indore, India

*Correspondence Info:

Dr. Bafna Angurbala,

Department of Biochemistry,

Govt. Holkar Science College, Indore, Madhya Pradesh, India

E-mail: balaindore@yahoo.com

Abstract

Cardiovascular disease is the leading cause of death for both men and women. Heart disease is not simple; many factors can contribute to a patient's overall heart health. Though more and more testing is available to help physicians to get an accurate picture of a patient's risks and treatment plan. Because of limited availability of instruments and financial assistance determination of each and every marker is difficult. We can assume the probable values of these markers by establishing regression equation. The objective of the study was to establish, regression equations among cardiovascular risk markers viz Albumin, TAC (Total antioxidant capacity), tHcy, Lp (a), LDL, HDL and TC.

Keywords: nephrotic syndrome, lipid profile, TAC, tHcy.

1. Introduction

Nephrotic Syndrome (NS) is the Glomerular disease with massive Proteinuria, Hypoalbuminemia and numerous other complications [1]. Among these complications saltwater retention, hyperlipidemia, metabolic bone disease, thromboembolism and infections are most important. Hypoalbuminemia were responsible for the progression of cardiovascular disease [2]. There is role for dyslipidemia in endothelial dysfunction and the risk for cardiovascular disease in NS [3]. Proteinuria hyperlipidemia, hypoalbuminemia, and very high level of Lp (a) was observed in the serum of nephrotic syndrome patients [4]. Significant correlations were found between PON (Paraoxonase), TAR (total antioxidant response), and total peroxide. Serum total protein was significantly positively correlated with PON and negatively correlated with total peroxide in acute-period NS patients [5]. tHcy and Lp (a) are reliable markers in the detection of extent of cardiac problem. An elevated plasma level of homocysteine (tHcy) was associated with increased risk of thrombotic, atherosclerotic vascular disease and endothelial dysfunction [6]. Hypoalbuminaemia in the nephrotic syndrome patients were resulted in increased oxidative activity, decreased antioxidant capacity and

hyperhomocysteinemia [7]. These markers are not easy to estimate. So, regression equation can be used to make their estimation easy. The objective of the study was to establish, regression equations among cardiovascular risk markers viz Albumin, TAC (Total antioxidant capacity), tHcy, Lp (a), LDL, HDL and TC.

2. Material and methods

For establishment of regression equations among cardiovascular risk markers, Nephrotic syndrome subject and Healthy subject were selected because they have varying values of these markers. Study was conducted from January 2007 to December 2009 on Nephrotic Syndrome patients at the Department of Biochemistry, Govt. Holkar Science College Indore (M.P.) with collaboration of Department of Biochemistry M.G.M. Medical College Indore (M.P.) India. The study was conducted on control and following two groups of NS-

Group 1 (Pre-treatment): In this group 105 Nephrotic syndrome patients were included.

Group 2 (Post-treatment): In this group 105 Nephrotic syndrome patients who are on remission after receiving standard oral corticosteroid induction

therapy for one month were included.

Control: In this group 99 normal healthy adults were included.

The patients were diagnosed on the basis of detailed clinical history; clinical examination and other relevant biochemical investigations. Biochemical parameters selected for present study were determined by using commercially available kit from Lab Kit diagnostics from Span in semi automated auto analyzer. LDL- Cholesterol level was calculated by using Friedewald's equation. Serum TAC was measured by the method described by Koracevic et al [8]. Serum MDA was measured by colorimetric method [9]. Lp (a) was estimated by a commercially available kit from human diagnostic kit method. Homocysteine was estimated by a commercially available kit from Keragen diagnostic kit method.

3. Results and Discussion

Following regression equations were obtained by using SPSS version after performing multiple regression analysis from the data obtained

Overall 43.3% relation exists between Albumin and TAC

$$\text{TAC} = 0.25x \text{albumin} + 0.801$$

Overall 27.7% relation exists between Albumin and HDL-C and is explained by the equation.

$$\text{HDL-C} = 5.73x \text{albumin} + 24.73$$

Overall 22.7% relation exists between tHcy and LDL-C and is explained by equation

$$\text{tHcy} = -0.027x \text{LDL-C} + 5.152$$

Overall 23.4% relation exists between tHcy and T C and is explained by equation.

$$\text{tHcy} = 0.025x \text{TC} + 3.473$$

Overall 18.6% relation exists between Lp (a) and TAC and is explained by equation.

$$\text{Lp (a)} = -43.001x \text{TAC} + 103$$

Overall 19.7% relation exists between Lp (a) and Albumin and is explained by equation.

$$\text{Lp (a)} = -16.81x \text{Albumin} + 87.48$$

Overall 20.1% relation exists between Lp (a) and TC and is explained by equation

$$\text{Lp (a)} = 0.187x \text{TC} - 17.396$$

Overall 21.1% relation exists between Albumin + HDL-C + zinc and tHcy and is explained by equation.

$$\text{tHcy} = -1.778 x \text{Albumin} - 0.055x \text{HDL-C} - 0.001x \text{Zinc} + 18.28$$

Overall 24.8% relation exists between Albumin + LDL-C and tHcy is explained by equation.

$$\text{tHcy} = 0.018x \text{LDL-C} - 0.977 x \text{albumin} + 9.879$$

Overall 23.1% relation exists between Lp (a) and Albumin + TAC and is explained by equation.

$$\text{Lp (a)} = -10.67x \text{albumin} - 24.56x \text{TAC} + 107.09$$

Overall 21.7% relation exists between Lp (a) and TC+HDL and is explained by equation.

$$\text{Lp (a)} = 0.153x \text{TC} - 0.529x \text{HDL-C} + 14.72$$

Overall 23.4% relation exists between tHcy and TC + Lp (a) and is explained by equation.

$$\text{tHcy} = 0.025 x \text{TC} + 0.000 x \text{Lp (a)} + 3.473$$

Overall 21.7% relation exists between Lp (a) and TC + HDL-C and is explained by equation.

$$\text{Lp (a)} = 0.153 x \text{TC} - 0.592 x \text{HDL-C} + 14.729$$

Overall 22.2% relation exists between Lp (a) and TC + LDL-C+HDL-C and is explained by equation.

$$\text{Lp (a)} = 0.337x \text{TC} - 0.217x \text{LDL-C} - 0.705x \text{HDL-C} + 13.578$$

The characteristic lipid abnormalities seen in the nephrotic syndrome include elevated very low-density lipoproteins (VLDL), low density lipoproteins (LDL), lipoprotein a [Lp(a)], cholesterol, and triglycerides, as well as normal or decreased serum levels of high density lipoproteins (HDL). The dyslipidemia associated with the nephrotic syndrome promotes accelerated atherosclerosis and increases cardiovascular risk in patients with persistent nephrotic syndrome. High Lp (a) concentration was observed that significantly contribute to the measured or calculated LDL-C level [10]. Severe atherosclerosis was also found in nephrotic syndrome, which was abdominal aortic syndrome (AAS) and abdominal aortic aneurysm (AAA). Markedly elevated Lp (a) plasma levels in patients had played an important role in the progression of atherosclerosis.

The above equations explain the overall relationship that exists among cardiovascular disease risk markers. These equations were supported by the result of following studies

- Reactive oxygen species (ROS) play a role in inducing the proteinuria in nephrotic syndrome (NS). Patients in the active phase of NS had significantly lower PON (Paraoxonase), and TAR (total antioxidant response) levels and higher Oxidative stress index (OSI) and total peroxide values than those in full remission. Significantly positive correlation with PON and negative correlation with total peroxide in acute-period NS patients [5].
- It is well established that, among plasma antioxidants, endogenous human serum albumin is considered the main extracellular molecule responsible for maintaining the plasma redox state [11].
- A positive correlation observed between albumin and HDL-cholesterol in cirrhosis. Simple measurement of serum albumin and HDL-C levels may be useful in identifying varying degrees of frailty. Serum albumin and HDL-C can be routinely used in older patients with low cholesterol to

distinguish three subgroups with different prognoses: (1) high risk: low albumin), (2) intermediate risk: high albumin and low HDL-C, and (3) low risk: high albumin and high HDL-C [12].

- There was a positive correlation ($p = 0.001$, $r = +0.431$) between the levels of homo-cysteine and total cholesterol [13].
- There was no significant correlation between tHcy and TGs and LDL-C levels. On the contrary, a negative relationship ($r = -0.42$) between tHcy and HDL-C concentration was found [14].
- The subjects with high tHcy levels which might impair the function of Apo-I and HDL and abnormal maturation of HDL particles although in presence of high ApoA-I levels would increase the risk of CAD [15].
- tHcy was negatively correlated with serum total protein and Albumin [16].

The mechanism through which elevated circulating level of tHcy cause vascular injury and promote thrombosis remain elusive [17]. During the autooxidation of tHcy in plasma, reactive oxygen species were generated. The later initiated lipid peroxidation in cell membranes (potentially responsible for endothelial dysfunction) in circulating lipoprotein, oxidized LDL-C, trigger platelet activation as well as some of the homeostatic abnormalities. In such patients, thus the oxidative stress induced by tHcy is a key process in the pathogenesis of thrombosis in NS.

4. Conclusion

By using these regression equations we can predict value of reliable markers of cardio vascular disease. tHcy and Lp(a) are reliable markers in the detection of extent of cardiac problem. These markers are not easy to estimate. So, these established regression equation can be used to predict their probable value easily.

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