Lipid Profile In Transplant Patients : A Clinical Study

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Abstract

15 renal transplant recipients were studied for their lipid profile. The patients were on regular post transplant follow up and had non clinical or laboratory evidence of graft dysfunction, intercurrent infection or post transplant diabetes mellitus for at least 3 months prior to the study. The mean duration of transplant was 15 ± 9.5 months (range 3-32 months). Majority (86%) were on triple immunosuppression therapy and received a mean prednisolone dose of 10.5 mg. An equal number of healthy subjects were randomly selected and studied for their lipid profile and served as control for the study group. There was no significant change in the HDL-cholesterol level as compared with controls. However, these patients showed a significantly higher LDL-cholesterol and total cholesterol levels. Further, a significant inverse correlation was observed between triglycerides and total cholesterol levels and transplant duration.

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Key Words : Lipid profile; Renal transplant

Introduction

Dyslipidemia is common in patients with renal disease [1-3]. Atherogenic changes in the level and composition of lipoproteins that are recognised as risk factors for cardiovascular diseases (CVD) in the general population occur in a majority of patients with renal disease [4-6]. The reported prevalence of dyslipidemia in renal transplant patients ranges from 16-72% depending on the patient population and the time point after transplantation when serum lipids were examined [7].

The pathogenesis of changes in lipid pattern in transplant patients is not clearly understood though it appears to be multifactorial. Perhaps the most important amongst these is, concomitant steroid and immunosuppressive therapy [8]. The present study was conducted to study the lipid profile in renal transplant patients with an objective to determine the nature of lipid abnormalities and also critically analyse the data to interpret its utility for therapeutic intervention.

Material and Methods

15 renal transplant recipients were studied. Patients with clinical and / or laboratory evidence of graft dysfunction, post transplant diabetes mellitus, any intercurrent infection and / or on antilipemic therapy were excluded from this study. The control group included 15 healthy subjects who attended out patient department for routine medical examination.

An informed consent was obtained from all patients before inclusion in this study. A detailed history was taken with emphasis on the economic status and dietary habits. The investigations performed included blood urea, creatinine, glucose, albumin, ECG and chest X-ray. After 14 hours of overnight fast, blood samples were collected for serum total

triglycerides (TG), total cholesterol (TC), low-density lipoprotein-C (LDL-C), high-density lipoprotein-C (HDL-C), and TC/HDL-C ratio. Specimens were analysed within 24 hours of collection.

All results were expressed, as mean $\pm$ SD. The significance was tested by Students 't' test. The Pearson's method was used to calculate correlation coefficient. Linear regression analysis was used to find the significance of lipid parameters with various clinical variables. Any value beyond 2 standard deviations of control group was considered significant.

Results

15 renal transplant recipients were studied for their lipid profiles from March 1998 to January 2000. The mean age was 33.6 years (range 26-44). There were 12 males and 3 females. The mean body mass index (BMI) was 21.4 ± 1.1 Kg/m². 67% patients were hypertensive with blood pressure $>140/90$ mm Hg. The mean systolic pressure was 144 ± 14 mm Hg and diastolic was 92 ± 6 mm Hg. The mean duration of renal transplant prior to study was 15 ± 9.5 months (range 3-32).

The antihypertensives used, included beta blockers (8 patients) and calcium channel blockers (4 patients). The immunosuppressive protocol consisted of cyclosporin (13 patients), azathioprine and prednisolone (all patients). The daily prednisolone dose was 10-12.5 mg (mean 10.5 mg). The clinical and biochemical characteristics of the control group are given in Table 1. There was no difference in the age and BMI as compared to the study group. None of the control group had hypertension and all had normal levels of serum creatinine, albumin and blood glucose.

Lipid profile : The mean $\pm$ SD values of serum TG, TC, LDL-C, HDL-C and TC/HDL-C ratio for the transplanted and control groups are summarized in Table 2. Elevated TC

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Table 1

Clinical and biochemical characteristics in renal transplant and control group

Group	n	Age (yrs) (range)	Sex	BMI Kg/m ²	Hypertension	Serum creatinine	Albumin g/dl	Glucose mg/dl
Transplant	15	33.6 (26-44)	M-12 F - 3	21.4 ± 1.1	10	0.9 ± 0.3	4 ± 0.2	101.7 ± 4.1
Control	15	40.3 (21-70)	M-10 F - 5	20.3 ± 1.4	0	0.8 ± 0.7	4 ± 0.6	90.2 ± 3.4

Values are Mean ± SD; n - Number of patients; BMI - Body mass index; M - Males; F - Females; BP in mmHg

Table 2

Serum lipid profile in renal transplant patients and comparison with controls

Group	TG (mg/dl)	TC (mg/dl)	LDL-C (mg/dl)	HDL-C (mg/dl)	TC/HDL-C
Transplant	157.9 ± 43.6** (103.0-248.0)	231.3 ± 35.9** (166.0-310.0)	131.8 ± 37.2** (72.0-205.0)	48.6 ± 10.5 (35.0-66.0)	5.0 ± 1.4 (2.8-8.6)
Control	87 ± 24.3 (43.0-136.0)	179.9 ± 12.6 (138.0-214.0)	103.1 ± 18.9 (68.0-136.0)	50.5 ± 8.2 (36.0-64.0)	3.6 ± 0.4 (2.9-4.7)

Values are mean ±SD (range in parenthesis); n - Number of patients; TC - Total cholesterol**; TG - Total triglycerides; LDL-C - Low density lipoprotein cholesterol; HDL-C - High density lipoprotein cholesterol; ** p < 0.001 versus control

Table 3

Sex wise distribution of serum lipid profile in renal transplant patients in comparison with controls

Group	n	TG (mg/dl)	TC (mg/dl)	LDL-C (mg/dl)	HDL-C (mg/dl)	TC/HDL-C
<i>Transplant</i>						
Male	12	158.7 ± 47.4	232.7 ± 37.7	139.3 ± 44.4	47.8 ± 11.3	5.1 ± 1.5
Female	3	154.3 ± 30.1	228.4 ± 31.7	129.9 ± 37.1	52.0 ± 6.5	5.4 ± 0.8
<i>Control</i>						
Male	10	88.7 ± 25.0	192.6 ± 19.3	106.1 ± 19.6	49.8 ± 8.0	3.7 ± 0.4
Female	5	85 ± 23.8	184.0 ± 21.0	97.3 ± 16.8	51.9 ± 8.8	3.5 ± 0.3

Table 4

Serum lipid profile in transplant patients in relation to duration post transplant

Transplant duration	n	TG (mg/dl)	TC (mg/dl)	LDL-C (mg/dl)	HDL-C (mg/dl)	TC/HDL-C
< 12 Months	10	173.6 ± 45.6	247.6 ± 31.6	148.2 ± 37.0	45.0 ± 6.2	5.6 ± 1.4
> 12 Months	5	139 ± 36*	212.5 ± 32.9*	118.6 ± 22.3	52.7 ± 13.2	4.3 ± 1.2

* p < 0.05

and LDL-C was observed in 60% and 33.3% respectively in the transplanted patients. The mean TC levels, TG levels and HDL-C levels were significantly higher in the transplant group (p < 0.001) when compared to controls (Table 3). These levels did not correlate with length of transplant period (Table 4). There was no abnormality in the levels of HDL-C in the renal transplant group.

Discussion

The present study was undertaken to study the lipid profile of renal transplant recipients. The results of this study demonstrated the occurrence of lipid abnormalities in renal allograft recipients and has further defined the pattern of hyperlipidaemia in these patients. Patients who undergo renal transplantation often have end stage renal disease (ESRD) for years and many of them already

have lipid derangement before transplantation [9]. After a successful renal transplant, though the renal function returns to normal, the lipid profile is reported to remain abnormal.

The prevalence of post transplant hyperlipidaemia ranges from 16-78% of recipients [10], depending at which time point post transplantation serum lipid levels were obtained. Hypercholesterolemia occurs within 6 months in most patients (82%), whereas the peak incidence of hypertriglyceridemia is at 12 months after transplantation [11]. In the present study, an inverse correlation was observed between TG and TC levels and transplant duration as shown in Table 3 and Fig 1. This observation is also in accordance with other studies [9,12,13]. The pathogenesis of hyperlipidaemia in renal

Fig. 1 : Correlation - Cholesterol and duration of transplant

Fig. 2 : Correlation - Triglyceride and duration of transplant

Fig. 3 : Correlation - Duration of transplant with TC & TG

transplant recipients is poorly understood and appears to be multifactorial. The numerous factors which have been shown to be associated with post transplant hyperlipidaemia include age, body weight, gender, pre-transplant lipid level, renal dysfunction, proteinuria, concomitant use of diuretics or beta blockers, diabetes mellitus, steroid use and cyclosporin use [8,11,14]. The relative contribution of these factors to the genesis of post transplant hyperlipidaemia is however unclear.

The association between immunosuppressive therapy and hyperlipidaemia has generally been observed early after transplantation and it remains a possibility that persistent hyperlipidaemia in the late post transplantation

period, is the result of factors other than immunosuppressive therapy [8]. CVD is the most common cause of post transplantation morbidity and mortality among long-term renal transplant survivors [10,15]. Patients with post renal transplantation coronary artery disease (CAD) tend to be older males, diabetic with higher cholesterol levels, greater incidence of smoking and greater number of acute renal allograft rejection episodes and as a consequence, have received more cumulative dose of steroids [16]. Several clinical studies have also reported correlation between hyperlipidaemia and chronic allograft rejection [8]. Increased serum TG levels have been implicated as the most consistent predictor of chronic allograft failure. This association between chronic allograft failure and hyperlipidemia may however, be a consequence rather than the cause of renal allograft failure [8]. Assessment of hyperlipidemia should be initiated soon after transplantation and should be followed by measurement of serum lipid concentrations once a year or earlier when indicated. The inverse correlation between lipid abnormalities and duration of transplant has certain therapeutic implications, in that, lipid profile in the first 8-12 months after transplantation is variable, it should not form the basis of therapy. The decision to treat hyperlipidaemia should be based on the lipid levels and the presence of positive risk factors for CAD including [17] age > 45 years in males, age >55 years in females, family history of premature CAD, current cigarette smoking, blood pressure >140/90 mm Hg despite antihypertensive therapy, HDL-C <35 mg/dl and diabetes mellitus. Because an increased LDL-C level is the most common lipid abnormality after renal transplantation, it is reasonable to follow the National Cholesterol Education Programme Guideline for treatment. Accordingly transplant recipients with LDL-C level of more than 130 mg/dl should be considered for pharmacologic treatment, especially if they have pre-existing CAD, diabetes or other risk factors [17].

In renal transplant recipients, a pattern of hyperlipidaemia occurs consisting of increase in TC, LDL-C and persistence of high triglycerides level. The pathogenesis of hyperlipidaemia in renal transplant recipient is poorly understood and appears to be multifactorial. Assessment of hyperlipidaemia should be initiated soon after transplantation and should be followed up by lipid level estimation once a year or earlier if indicated. The decision to treat hyperlipidaemia is indicated in patients with LDL-C level greater than 130 mg/dl especially if they have pre-existing CAD, diabetes or other risk factors.

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