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Original Article

Assessment of Coronary Blood Flow in Children with Chronic Renal Failure on Regular Hemodialysis

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ABSTRACT

Background: Coronary flow reserve (CFR) reflects the functional capacity of the microcirculation to adapt to blood demand during increased cardiac work. Diminished CFR may account for several symptoms that are often encountered in haemodialysis patients such as chest pain, arrhythmia and hypotension. lschemic heart disease is by far the leading cause of morbidity and mortality in haemodialysis (HD) patients. Since prevention is not easy, early detection of the disease is the key issue.

Objectives: Assessment of coronary flow reserve in children with chronic renal failure on regular hemodialysis with transthoracic Doppler echocardiography using dipyridamole as and inducer of coronary hyperemia.

Methods: Sixty children of matching age and sex were included in this study, 20 healthy children as a control group and 40 children with chronic renal failure on regular haemodialysis. All studied children were subjected complete history taking, thorough clinical examination, laboratory investigations and assessment of coronary flow reserve with transthoracic Doppler echocardiography using dipyridamole as inducer of coronary hyperemia.

Results: There was a significant negative correlation between CFR and LVMI, duration of dialysis, serum cholesterol, triglycerides, LDL levels and blood pressure in hemodialysis patients. A significant positive correlation between CFR and serum IIDI. level was found. There was no significant correlation between CFR and different laboratory parameters.

Conclusion: CFR is significantly reduced in children with CAF on regular hemodialysis. Control of blood pressure, correction of anemia and hypervolemia, diet management and physical activity are important in the prevention of / decrease in or improving the coronary flow reserve (CFR).

INTRODUCTION

Ischemic heart disease is by far the **leading cause of morbidity and mortality in hemodialysis (HD) patients. Since prevention is not easy, early detection of the disease is the key issue'). Impairment of coronary microvasc .lar functions and decreased coronary flow reserve (CFR) detected by transthoracic Doppler echocardiography (TIDE) has recently been** reported in itemodfislysis patievtst`). Coronary flow reserve reflects the functional **capacity of microcirculation to adapt to blood demand during increased cardiac work. It has been shown to be highly sensitive and specific in the general population. Diminished coronary flow reserve may account for several symptoms that are often encountered in haemodialysis patients. Chest pain, arrhythmia and hypotension**

during haemodialysis sessions may be Caused by diminished coronary flow[ir.

AIM OF THE WORK

Assessment of coronary flow reserve in children with chronic renal failure on regular hemodialysis with transthoracic Doppler echocardiography using dipyridamole as an inducer of coronary hyperemia.

SUBJECTS AND METHODS

This cross section observational case control study was conducted in the pediatric nephrodialysis and echocardiography units of Zagazig University Hospital in the period from April 2009 to April 2010. This study passed the ethical committee issue.

Sixty patients were included in this study; they were classified into two groups:

1. Group A "control group":
   This group comprised 20 healthy children attending the pediatric outpatient clinic in Zagazig University (12 male and 8 female) their ages ranged from 3 to 13 years. They were apparently healthy with clinical examination. They had no history of chronic illness and did not receive any medications.
2. Group B "cases group":
   This group comprised 40 children with chronic renal failure on regular hemodialysis; they were 24 males and 16 females their ages ranged from 2 to 16 years.
   Hemodialysis protocol was thrice weekly for a 3 to 4 hrs period every session with a standard citrate containing dialysate bath, using biocoi rpatible HD membrane (Polysulphone, FX-80 series, Fresenius, Germany). Blood flow rates ranged from 180 to 250 ml/min. They were 24 males and 16 females their ages ranged from 2 to 16 years.

Exclusion criteria:

All patients with the following conditions were excluded from the study:

1. Acute renal failure.
2. Hemoglobin level below 8 gm/dl.
3. Central venous line as a route of dialysis.
4. Bronchial asthma.
5. Cardiac arrhythmia.
6. Congestive heart failure.
7. Congenital heart disease.
8. Patients whose anterior descending coronary artery couldn't be visualized adequately with Doppler echocardiography.

All studied children were subjected to the following:

1. Complete history taking as regarding age and sex, duration of dialysis, cause of chronic renal failure. symptoms of cardiovascular problems (e.g. palpitation, dyspnoea and chest pain with stress on position, referral, duration, timing, if improved with medication).
2. l'horough clinical examination including blood pressure, heart rate, pallor, signs of cardiomegaly (apical shift and pulsations), musculo-skeletal problems, bleeding and infection.
3. Laboratory investigations including complete blood count, serum creatinine and blood urea nitrogen, calcium, phosphorus and parathormone levels, serum cholesterol, triglycerides, iron, ferritin, albumin and high-sensitivity C-reactive protein (hs-CRP) levels.
   Samples of venous blood were withdrawn from all subjects in the early

morning before dialysis and collected in calcium free tubes, left at 37°C until clot retraction. Clear sera were separated after centrifugation at 2000 for 15 minutes divided and stored at - 20°C.

4. Echocardiographic assessment was done for all subjects with vivid 7 GE apparatus using multi-frequency matrix (M3S) probe.

- *Coronary flow reserve measurement:*

The acoustic window was around the mid-clavicular line in the fourth and fifth intercostal spaces in the left lateral decubitus position. The left ventricle was imaged in the cross section view and the ultrasound beam was inclined laterally. The coronary blood in the mid to distal left anterior descending coronary artery was examined by color Doppler flow mapping guidance with the optimal velocity range (+ 12 to + 15 cm/sec.) then the sample volume (1.5 or 2 mm wide) was positioned on the color signal in the left anterior descending coronary artery[3]

Variables of the left anterior descending coronary artery velocity were measured by using fast Fourier transformation analysis. After base line recording of flows, dipyridamole (0.56 mg/Kg: Persantin, Boehringer-Ingelheim) was infused over 4 minutes. Ten minutes after the end of infusion, hyperemic spectral profiles ih the left anterior descending coronary artery were recorded.

All images were recorded by playback analysis and were later measured offline.

Average diastolic peak flow velocity (APFV) and average mean diastolic flow velocity were measured at baseline and under hyperemic conditions.

Coronary flow reserve was defined as APFV at hyperemia to APFV at baseline. CFR > 2 was considered normal[5].

- *Left ventricular mass index* was calculated from M-mode records taken on parasternal long axis images according to Devereux's formula[4] considering the diastolic measurements of left ventricular internal diameter (LVID), interventricular septal thickness (IVST) and posterior wall thickness (PWT).

$LVMI\ (g/m^2) = (1.04\ [(IVST + LVID + PWT)^3 — LVID^3] — 14\ g) /$ Body surface area.

The pulsed Doppler transmitral flow velocity was recorded to measure the ratio of peak mitral E-wave velocity to peak mitral A-wave velocity (E/A ratio) and the deceleration time of mitral E-wave velocity.

All patients had continuous heart rate and ECG monitoring throughout this examination. Blood pressure was recorded at baseline, during dipyridamole infusion, and at recovery.

All measurements were performed between 1 and 3 pm and all of the subjects abstained from caffeine-containing drinks for at least 12 hr before testing. Transthoracic Doppler echocardiography (TIDE) examinations were performed on the day of dialysis in all HD patients after dialysis sessions.

Statistical analysis: Continuous data are expressed as the mean value + SD (range). Differences between two different parametric variables at rest and during hyperemia were bested using the paired, two-tailed Studelft t test. Analysis of variance (Anova) F test and subsequently

the post-hoc F test (least significant difference) were performed to compare parametric variables among three groups. The chi-square test was used to analyze the incidence of non-parametric data. A p value < 0.05 was considered significant. Correlation between continuous parameters was evaluated using linear regression analysis. Data was analyzed using SPSS (Statistical Package for Social Sciences) version 11 [٢].

RESULTS

Results of this study are summarized in Tables 1 - 18 and illustrated in Figures 1 - 12. CFR is significantly reduced in children with CRF on regular hemodialysis in contrast to control group as shown in Table (6). This decrease is significantly negatively correlated with LVMI, duration of dialysis, serum level of cholesterol, triglycerides, LDL, blood pressure and CRP as shown in Tables (11, 12, 13, 15, 18) and Figures (3, 4, 5, 6, 7, 10 and 12) respectively. Table (7) shows no significant change in blood pressure of the studied groups before and after dipyridamole infusion. Table (10) shows no significant correlation between CFR and different laboratory markers.

Table 1: Characteristics of the studied group.

	Cases No. = 40	**Control No. = 20**	**Significance**
Age:			
$\overline{X} \pm SD$	10.3 ± 4.4	8.7 ± 3.7	p = 0.16
Range	2-16	3-13	
Sex:			
Male	24 (60%)	12 (60%)	p = 1.0
Female	16 (40%)	8 (40%)	
Duration of dialysis (in years)			
$\overline{X} \pm SD$	2.49 ± 1.9		
Range	1 - 7 yrs		

Table 2: The underlying etiology of chronic renal failure in the studied group.

Etiology	No.	%
Familial Mediterranean fever	1	2.5
Steroid resistant nephrotic syndrome	4	10
Focal segmental glomerulosclerosis	7	17.5
Unknown	14	35
Chronic familial interstitial nephritis	2	5
Sickle cell nephropathy	1	2.5
Neurogenic bladder	2	5
Chronic interstitial nephritis	2	5
Diffuse proliferative glomerulonephritis	1	2.5
Rapidly progressive glomerulonephritis	1	2.5
Vesicouretric reflux	3	7.5
Juvenile nephronophthisis	1	2.5
Membranoproliferative glomerulonephritis	1	2.5
Total	40	100.0

Table 3: Clinical data of studied group on haemodialysis.

Clinical manifestation	Number of cases (Total = 40 case)	%
Blood pressure (BP):		
Hypertensive	26	65
controlled on medications	6	15
uncontrolled	20	50
Hypotensive	10	25
Normotensive	4	10
Cardiomegaly	25	62
Chest pain	6	15
Tachycardia	11	27

Table 4: The laboratory parameters of the studied groups.

	Cases (No. = 40) on haemodialysis		Control (No. = 20)		p value
	M ± SD	Range	M ± SD	Range	
ALB (g/dl)	3.6 ± 0.38	2.9 - 4.4	3.67 ± 0.2	3.5 - 4	0.001** HS
BUN (mg/dl)	56.1 ± 11.3	40 - 84	12.4 ± 3.4	8 - 18	0.001** HS
Creatinine (mg/dl)	5.8 ± 2.3	1.8 - 12	0.5 ± 0.09	0.3 - 0.6	0.001** HS
HB (g/dl)	9.5 ± 1.26	7.1 - 13.7	11.6 ± 1	10 - 13	0.001** HS
Platelets Count / cmm	243.77 ± 83.92	38 - 424	227.50 ± 96.07	100 - 400	0.611
Ca (mg/dl)	7.6 ± 1.6	5 - 9.5	10.10 ± 0.65	9 - 11	0.001** HS
Pi (mg/dl)	5.83 ± 1.8	3.1 - 9.3	3.4 ± 1.8	2.8 - 4.5	0.001** HS
$Ca^{*}PO_4$ product	41.65 ± 20.1	15 - 72	30 ± 9.2	18 - 44	0.09
Fe (mg/dl)	74.4 ± 38.7	21 - 165	91 ± 18.4	60 - 120	0.19
PTH (pg/ml)	366.1 ± 267	27 - 950	27.1 ± 16	7 - 53	0.001** HS
Ferritin (ng/ml)	1076 ± 881	125 - 3200	130 ± 31.9	70 - 170	0.002** HS
CRP (mg/dl)	15.8 ± 8.96	2 - 22	1.5 ± 1.3	0 - 4	0.001** HS
Cholesterol (mg/dl)	154 ± 39	100 - 230	151 ± 4.76	144 - 160	0.78
Triglycerides (mg/dl)	158 ± 90.7	50 - 330	52 ± 1.9	50 - 55	0.001** HS
LDL (mg/dl)	171 ± 20.3	140 - 200	75 ± 10.4	5 -100	0.001** HS
HDL (mg/dl)	44.5 ± 6.6	30 - 53	52.3 ± 3.4	49 - 58	0.001** HS

Table 5: The echocardiographic parameters of the studied groups.

	Cases	Control	p-value
LVED (cm)			
M ± SD	4.1 ± 0.8	3.38 ± 0.5	0.001** HS
Range	2.9-5.2	2.8-4.2	
LVES (cm)			
M ± SD	2.5 ± 0.6	2.16 ± 0.3	0.005* S
Range	1.7-4.1	1.2-2.6	
IVS (cm)			
M ± SD	1.005 ± 0.25	0.74 ± 0.13	0.001** HS
Range	0.6-1.6	0.6-1	
PWT (cm)			
M ± SD	1.006 ± 0.38	0.78 ± 0.13	0.002* S
Range	0.4-1.7	0.6-1	
FS (%)			
M ± SD	37 ± 4.7	39.8 ± 5.9	0.05* S
Range	22-47	30-50	
EF (%)			
M ± SD	58.20 ± 3.28	70.40 ± 6.6	0.001** HS
Range	53-64	65-85	
E/A			
M ± SD	1.33 ± 0.27	1.49 ± 0.18	0.017* S
Range	0.77-1.76	1.14-1.73	
LVMI (g/sq. m)			
M ± SD	168.2 ± 47	84.9 ± 35.3	0.001** HS
Range	75-300	20-123	

LVED = left ventricular end diastolic dimension.
LVES = left ventricular end systolic dimension.
IVS = inter ventricular septum in diastole.
PWT = posterior wall thickness in diastole.
FS = fraction of shortening.
EF = ejection fraction.
E/A = ratio of peak mitral E-wave velocity to peak mitral A-wave velocity.
LVMI = left ventricular mass index.

Table 6: The hemodynamics and coronary flow parameters of the studied groups.

	Cases	Control	p-value
Baseline			
S.B.P. (mmHg)			
M ± SD	124 ± 23	104.3 ± 8.9	0.001** HS
Range	90-165	90-115	
D.B.P. (mmHg)			
M ± SD	80 ± 15.7	67.7 ± 5.1	0.001** HS
Range	50-105	60-75	
Heart rate			
M ± SD	105 ± 7.7	92.9 ± 8	0.001** HS
Range	90-120	80-110	
APFV (cm/sec)			
M ± SD	52.3 ± 5.1	24.4 ± 3.6	0.001** HS
Range	40-61	19-29	
Hyperemia			
S.B.P.			
M ± SD	120.9 ± 2.6	103 ± 8.8	0.001** HS
Range	90-155	89-110	
D.B.P.			
M ± SD	77 ± 14.5	67.2 ± 6.9	0.005* S
Range	50-100	55-80	
Heart rate			
M ± SD	107 ± 8.3	94 ± 9.2	0.001** HS
Range	95-123	80-109	
APFV			
M ± SD	52.3 ± 5.12	62 ± 6.15	0.002* S
Range	45-61	48-69	
CFR			
M ± SD	1.63 ± 0.14	2.63 ± 0.34	0.001** HS
Range	1.3-1.8	2.3-3	

S.B.P. = systolic blood pressure
D.B.P. = diastolic blood pressure
APFV = average peak flow velocity
CFR = coronary flow reserve

Table 7: Haemodynamic parameters of studied groups before and after dipyridamole infusion.

	Before	After	p-value
S.B.P. (mmHg)			
Cases	124 ± 23	120.9 ± 20.6	0.08
Control	104 ± 8.9	103 ± 8.8	0.06
D.B.P. (mmHg)			
Cases	80 ± 15.7	77 ± 14.5	0.06
Control	67.7 ± 5.1	67.2 ± 6.9	1.0
Heart rate			
Cases	105.5 ± 7.7	107.7 ± 6.3	0.06
Control	92.9 ± 8	94 ± 9.2	0.06

Table 8: The relation of blood pressure groups to LVMI and CFR.

	Blood Pressure			p
	Hypotensive (No. = 10) A	Normotensive (No. = 4) B	Hypertensive (No. = 26) C	
CFR				
M ± SD	1.76 ± 0.048	1.73 ± 0.04	1.56 ± 0.13	0.001** HS
Range	1.69-1.8	1.7-1.8	1.3-1.78	
LVMI (g/m^2)				
M ± SD	141.2 ± 36.3	162.5 ± 19	179.1 ± 33.7	0.04* Sig.
Range	120 ± 200	140-180	75-300	

Least significant difference between groups A, B – B, C – A, C

CFR
A versus B → p = 0.8
A versus C → p = 0.001** HS
B versus C → p = 0.02* Sig.

LVMI
A versus B → p = 0.4
A versus C → p = 0.001** HS
B versus C → p = 0.01* Sig.

Table 9: Percentage of patients with severely impaired CFR.

CFR	No. of cases	%
< 1.5	10	25
> 1.5	30	75
Total	40	100

Table 10: Correlation between CFR and different laboratory markers.

	r	p	Sig.
BUN (mg/dl)	-0.13	> 0.05	NS
Creatinine (mg/dl)	-0.63	> 0.05	NS
Haemoglobin (g/dl)	0.001	> 0.05	NS
Albumin (g/dl)	0.03	> 0.05	NS
Calcium (mg/dl)	0.13	> 0.05	NS
Phosphorus (mg/dl)	0.18	> 0.05	NS
Ca^{*} PO_4 product	-0.17	> 0.05	NS
Iron (mg/dl)	0.19	> 0.05	NS
Ferritin (ng/ml)	-0.13	> 0.05	NS
PTH (pg/ml)	-0.04	> 0.05	NS

Table 11: Correlation between CFR and LVMI.

	r	p	Sig.
Cases	-0.58	< 0.001	HS
Control	0.11	> 0.05	NS

Table 12: Correlation between CFR and duration of dialysis.

	r	p	Sig.
Duration of dialysis	-0.9	< 0.05	Sig.

Table 13: Correlation between CFR and lipid profile.

	r	p	Sig.
Cholesterol	-0.69	<0.001	HS
Triglycerides	-0.8	<0.001	HS
HDL	0.52	<0.001	HS
LDL	-0.6	0.001	HS

Table 14: Correlation between blood pressure and LVMI.

	r	p	Sig.
LVMI	0.58	0.001	HS

Table 15: Correlation between CFR and blood pressure.

	r	p	Sig.
CFR	-0.49	0.001	HS

Table 16: Correlation between CFR and E/A ratio.

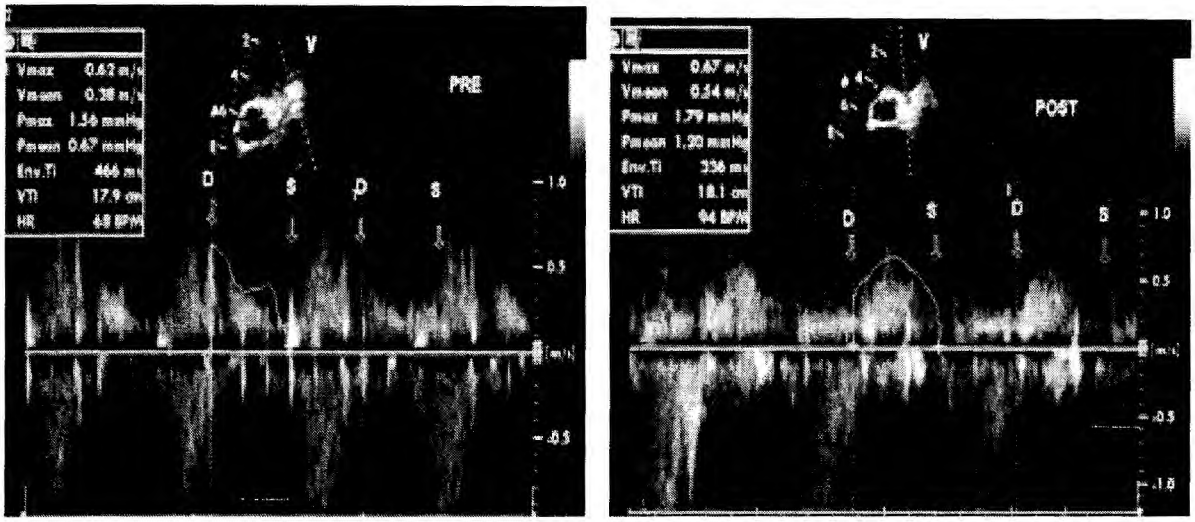
	r	p	Sig.
E/A	-0.21	>0.05	NS

Table 17: Correlation between basal APFV and hemoglobin level.

	r	p	Sig.
Hb	-0.56	<0.05	Sig.

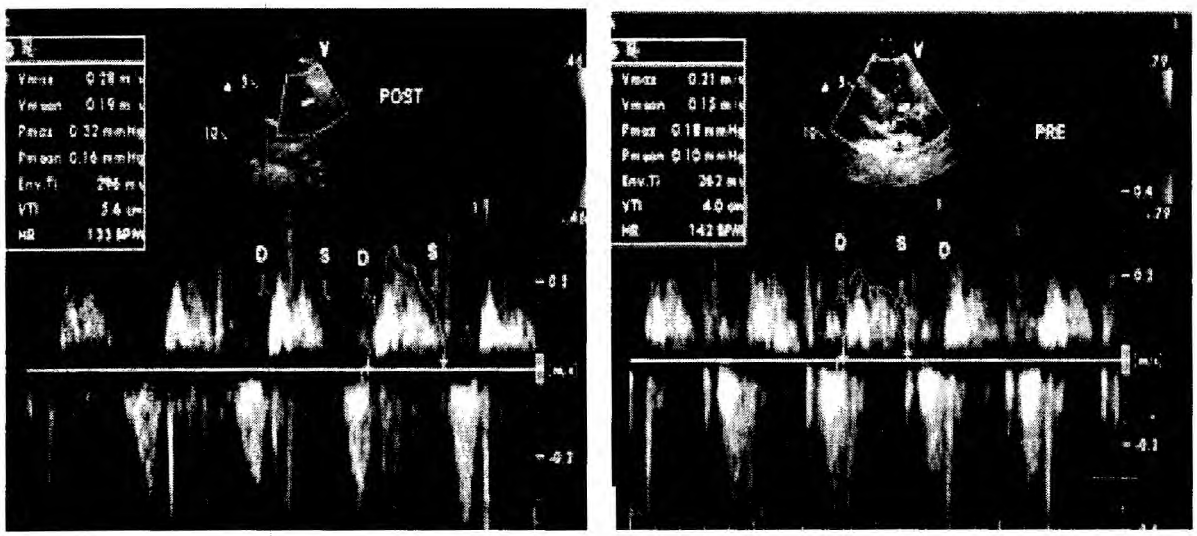
Table 18: Correlation between CFR and CRP.

	r	p	Sig.
CRP	-0.88	<0.001	HS



Rest Dipyridamole

Fig. 1: An example of coronary flow velocity recording in LAD coronary artery at rest and during hyperemia in HD patient.



Rest Dipyridamole

Fig. 2: An example of coronary flow velocity recording in LAD coronary artery at rest and during hyperemia in control subject.

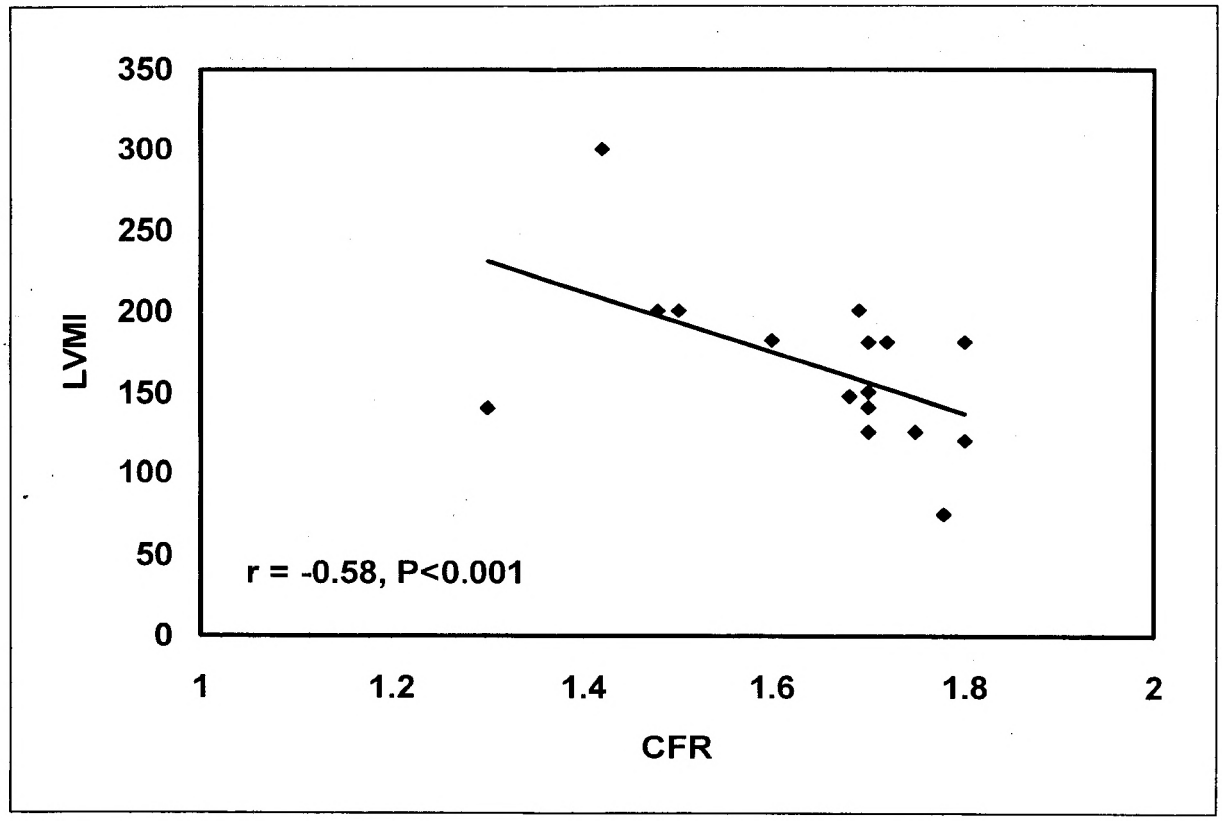


Fig. 3: Correlation between CFR and LVMI.

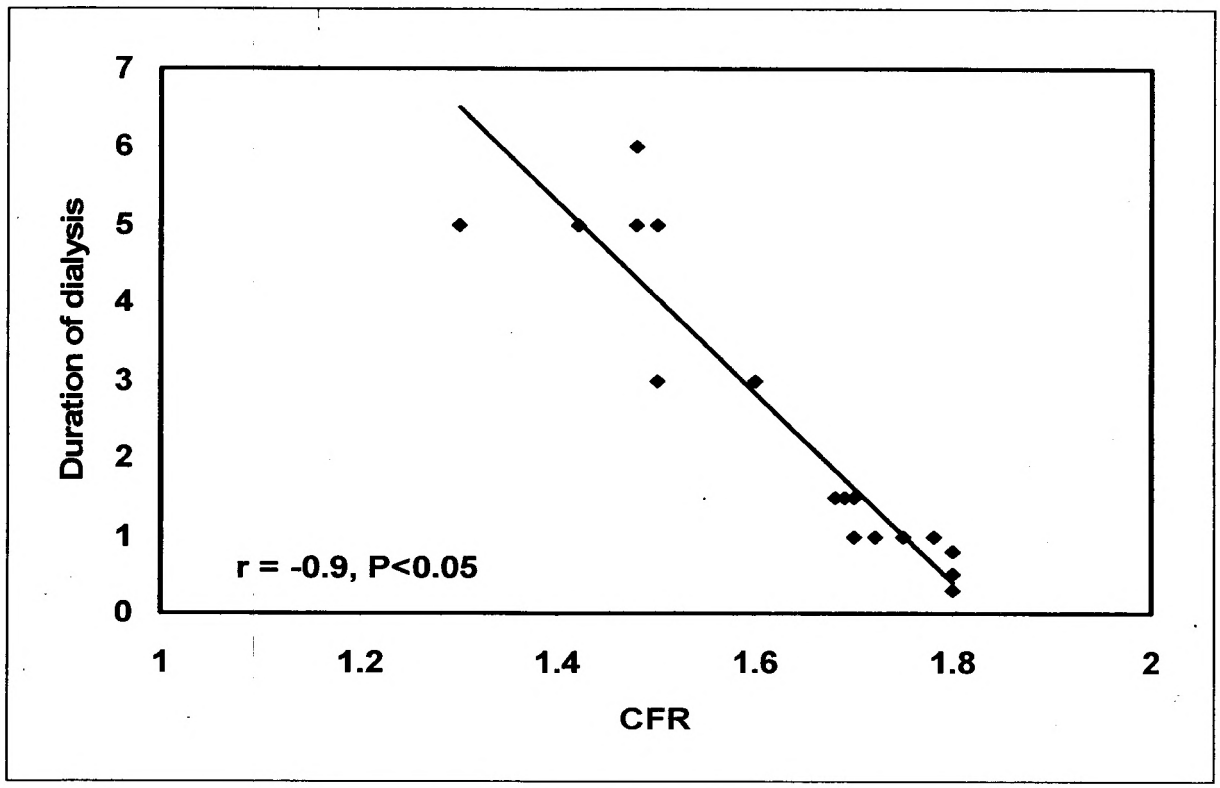


Fig. 4: Correlation between CFR and duration of dialysis.

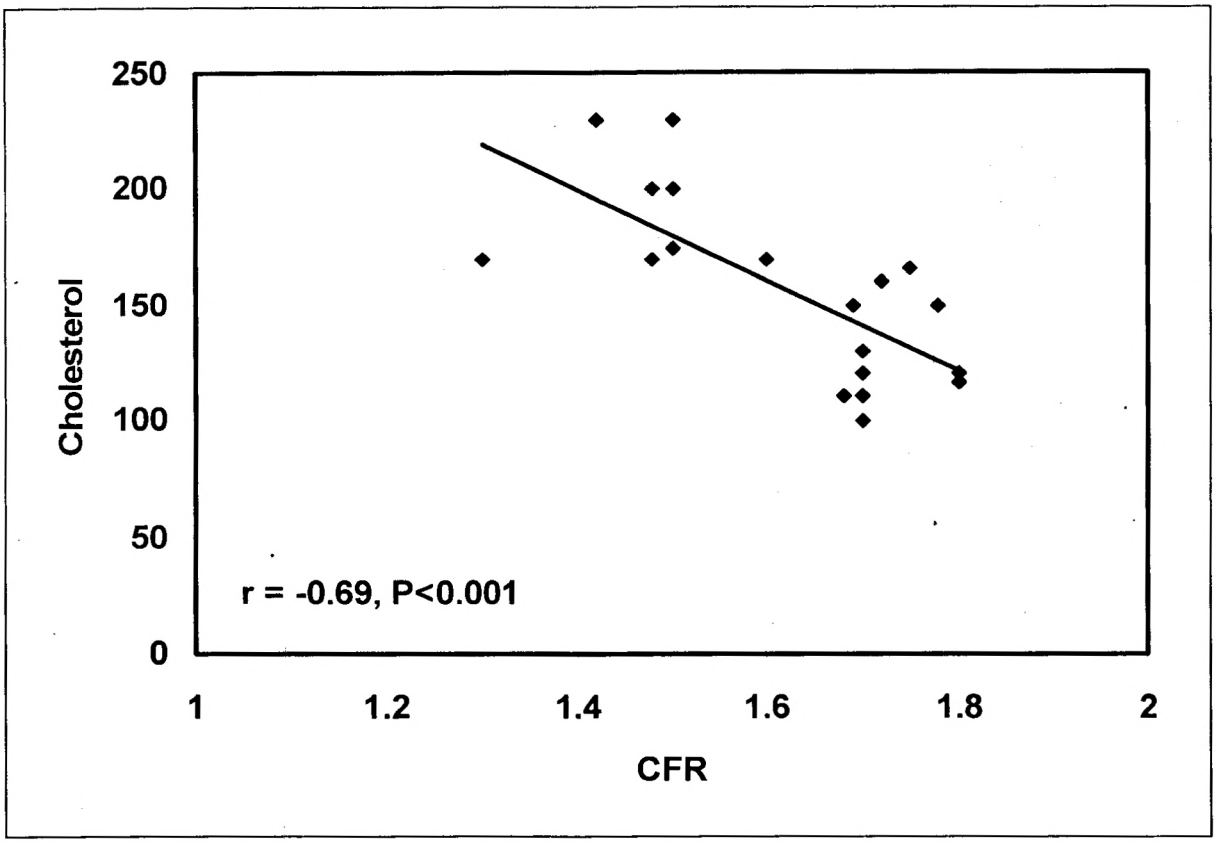


Fig. 5: Correlation between CFR and cholesterol.

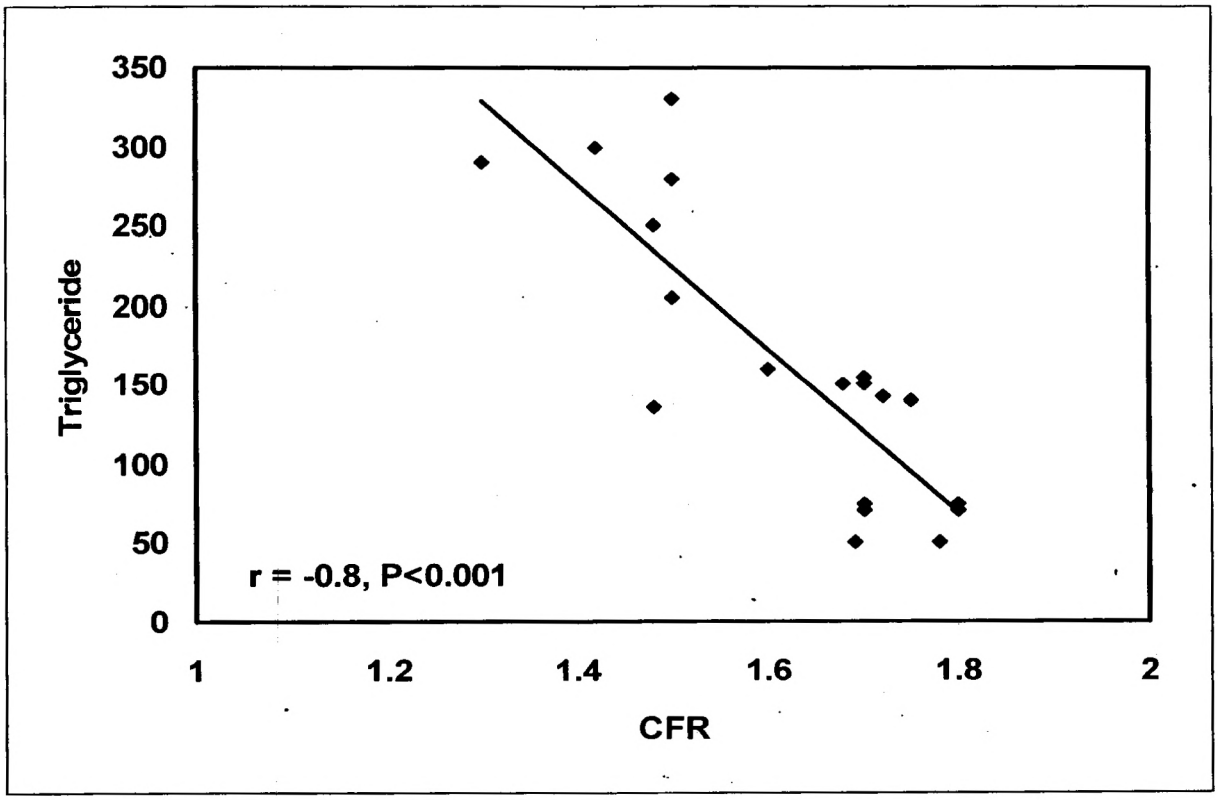


Fig. 6: Correlation between CFR and triglycerides.

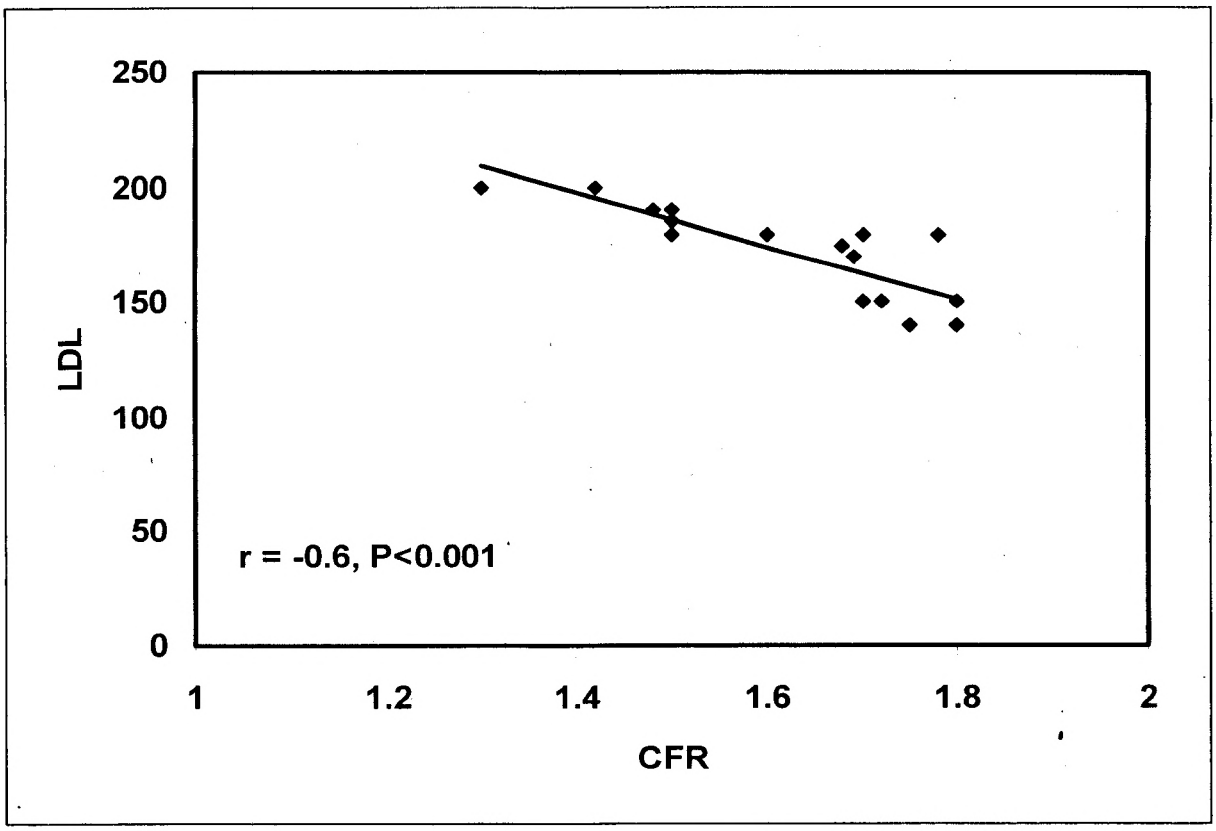


Fig. 7: Correlation between CFR and LDL.

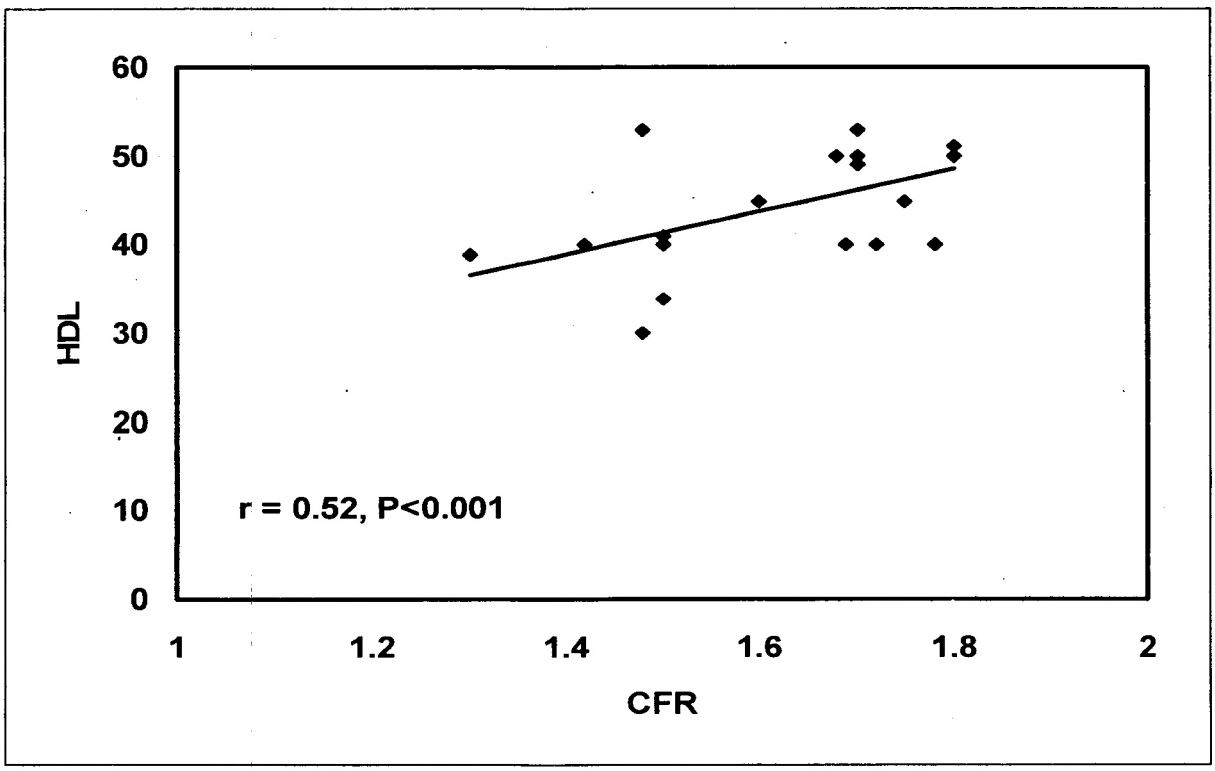


Fig. 8: Correlation between CFR and HDL.

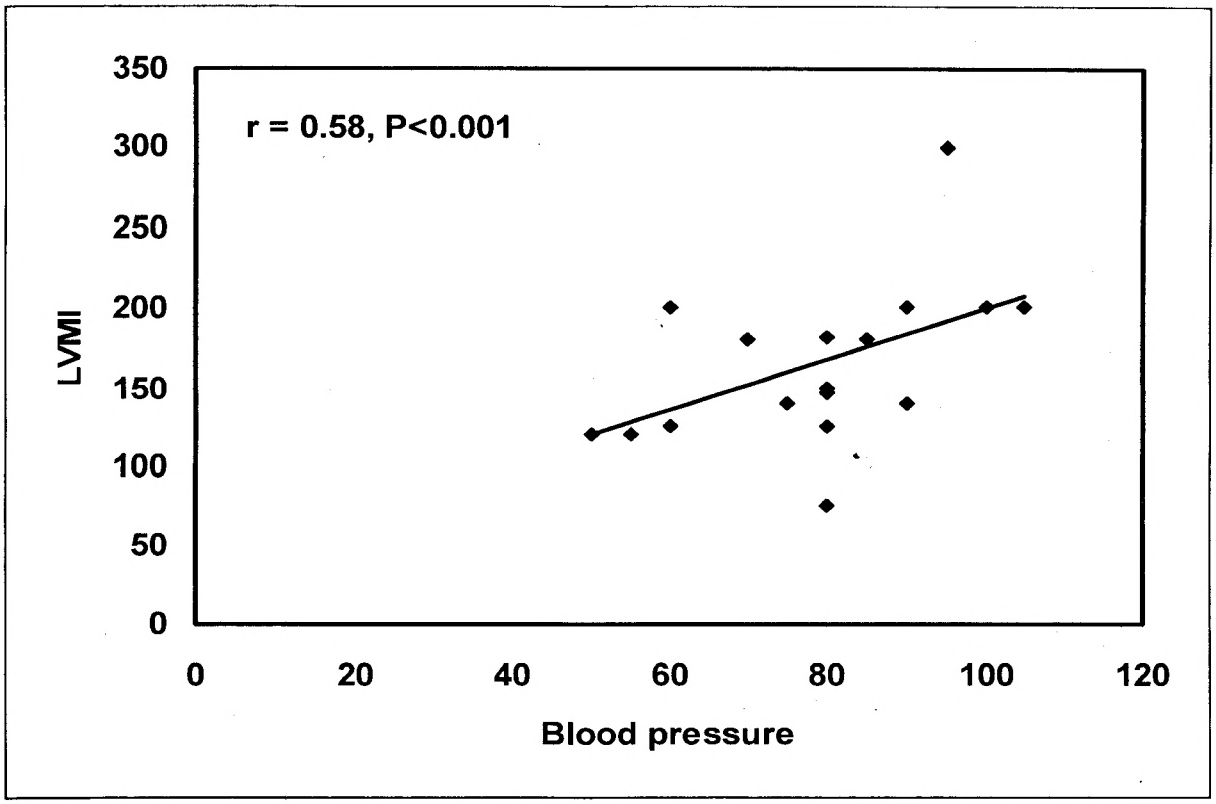


Fig. 9: Correlation between blood pressure and LVMI.

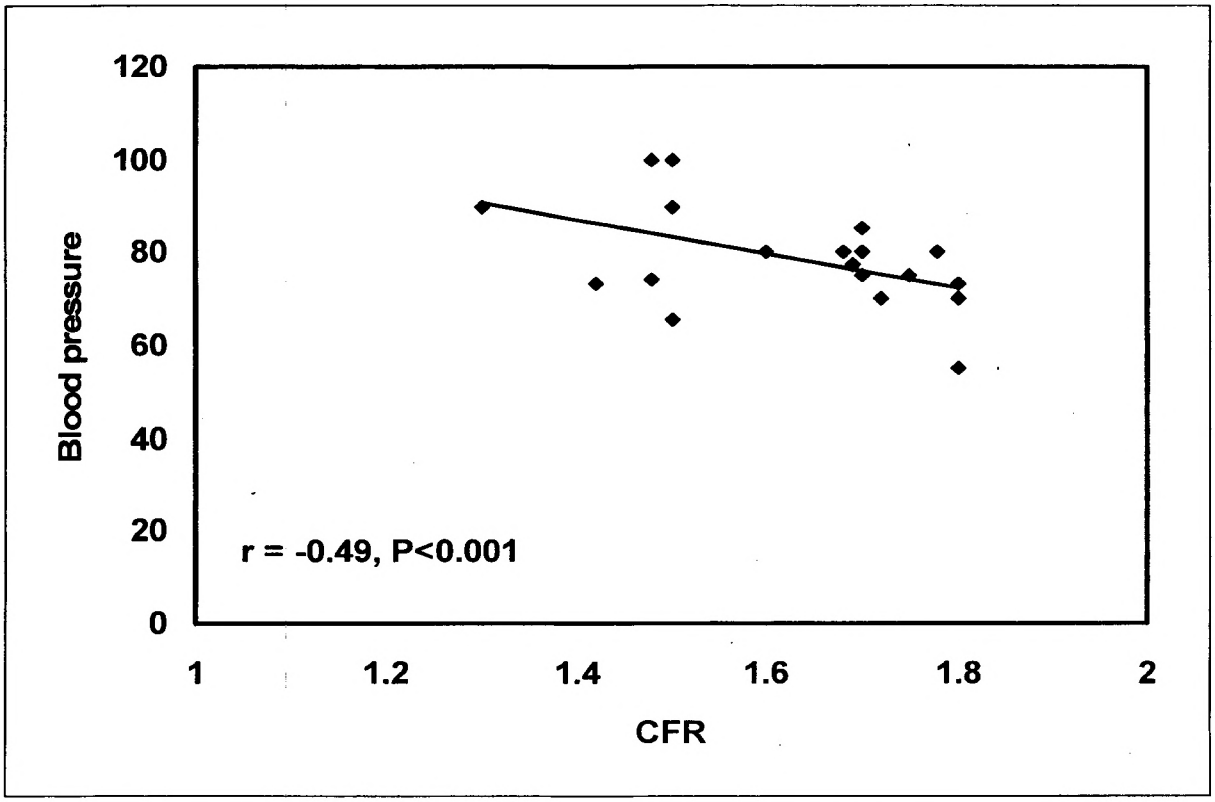


Fig. 10: Correlation between CFR and blood pressure.

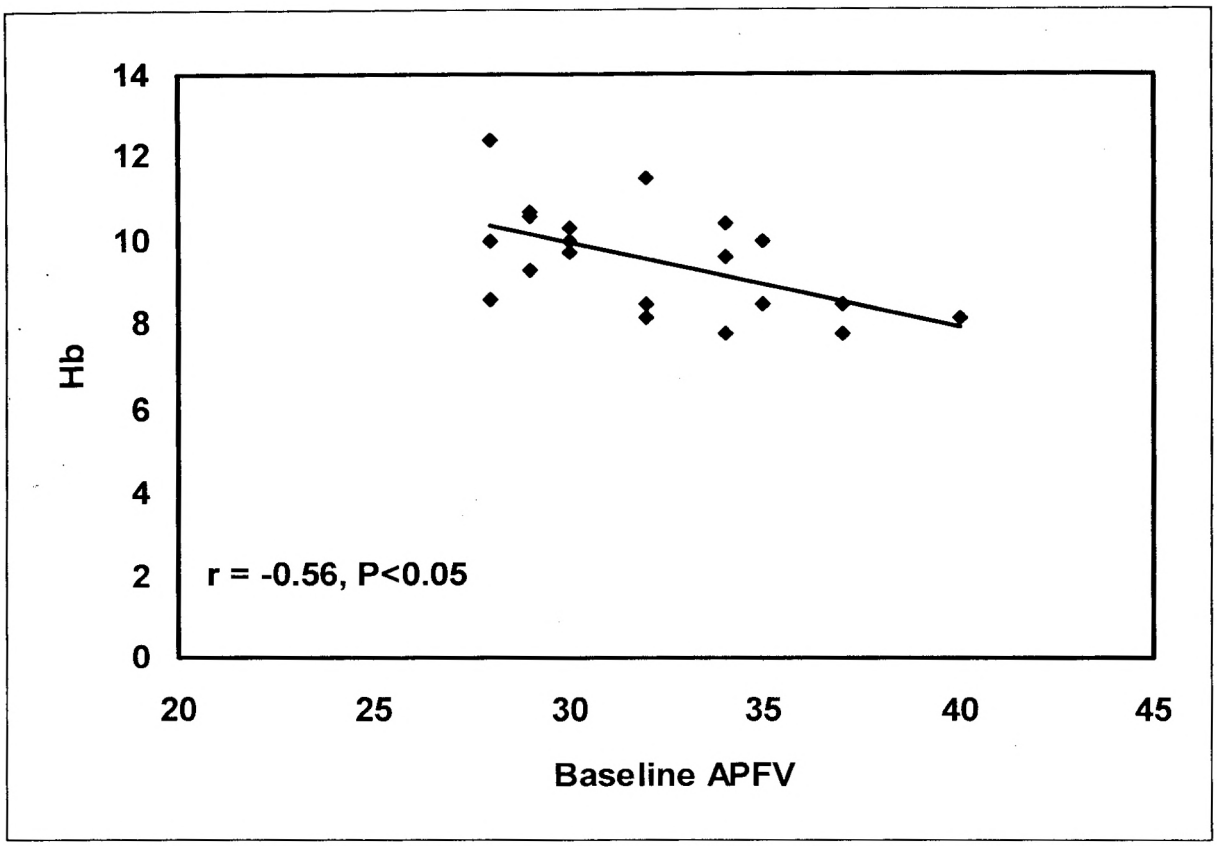


Fig. 11: Correlation between baseline APFV and HB.

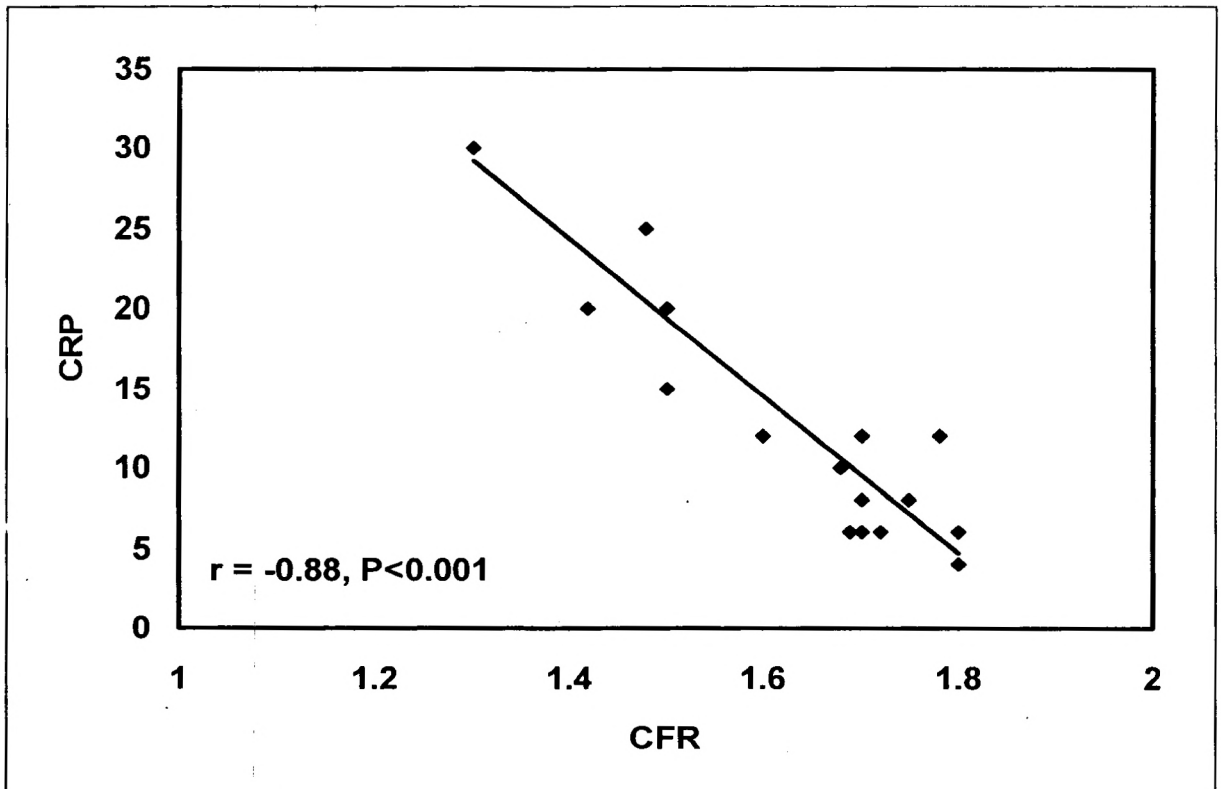


Fig. 12: Correlation between CFR **and CRP.**

DISCUSSION

Cardiovascular diseases are a leading cause of death in end-stage renal disease (ESRD) largely as a result of the broad constellation of uremia-associated factors that can adversely affect cardiac function. Hypertension, one of the leading causes of renal failure, is a major culprit in this process, causing left ventricular hypertrophy, cardiac chamber dilation, increased left ventricular wall stress, redistribution of coronary blood flow, reduced coronary artery vasodilator reserve, ischemia, myocardial fibrosis, heart failure, and arrhythmias[6]. Coronary flow reserve is an integrating measure of endothelial function, vascular smooth muscle relaxation and epicardial stenosis[7].

Reduced CFR is an important feature of hemodialysis patients with hypertrophied ventricle. Although this reduced CFR may not affect left ventricular function at rest, it could cause impaired subendocardial wall function and reduced subendocardial coronary perfusion during periods of stress in the hypertrophied myocardium. Repeated stress and subendocardial ischemia lead to subendocardial fibrosis, which also impairs systolic function then accelerate the progression from compensated left ventricular hypertrophy to failure).

In this study we aimed at assessing the coronary flow reserve in children on regular hemodialysis which reflects the functional capacity of microcirculation to adapt to blood demand during increased cardiac work.

Significant reduction of coronary flow reserve was observed in our haemodialysis patients (1.63 i 0.14 versus 2.63 ± 0.34, p = 0.001). This is because the average peak coronary flow velocity (APFV) at baseline in HD patients was significantly greater than that in control subjects, and the average peak coronary flow velocity during hyperemia was significantly lower in haemodialysis group than that in control subjects. This is in agreement with the findings of Robinson et al. (2007)[5] who also stated that the elevated APFV at baseline may be attributed to an increase in left ventricular mass due to long-standing hypertension and anemia, which are common in these patients population as myocardial blood flow at rest depends on oxygen demand which in turn is related to cardiac work. While reduced APFV at hyperemia may be attributed to endothelial dysfunction which is thought to he a key initial event in the development of atherosclerosis which leads to loss or reduction in the effect of the nitric oxide. Also presence of coronary artery calcifications (GAGS) may represent an inappropriate vasodilatory response to pharmacological stimulus due to the accumulation of calcium in the media layer. In addition, calcium deposition in the intima, which may impair endothelial function, could be another possible mechanism for decreased CFR. Therefore, it is not clear whether CFR impairment (failure of coronary artery vasodilatation to pharmacological stimulus) is due to medial calcification or endothelial dysfunction itself.

Also, supporting the findings of our study, Tok et al. (2005)[10] reported that coronary flow reserve was impaired in haemodialysis patients (2.03 + 0.3 vs. 2.61 H 0.5, p = 0.005). On the same hand, Niizuma et al. (2008)m studied the prevalence and

mechanism of abnormal CFR in HD patients without significant LAD coronary artery stenosis detected with angiography and found diminished coronary flow reserve in haemodialysis patients and this is because the average peak coronary flow velocity at baseline in HD patients was significantly greater than that in control subjects. The average peak coronary flow velocity during hyperemia tended to be greater in the haemodialysis group than in control subjects, but this difference was not statistically significant. While Koivuviita et al. (2009)[11] found that the basal myocardial perfusion was statistically significantly higher in CKD patients than observed values in similarly aged controls, but coronary flow reserve was normal although baseline myocardial blood flow was increased in all CKD patients as compared to healthy controls which is opposite to our results.

In our study left ventricular hypertrophy as assessed by the LVMI was significantly higher in HD patients than in control group (168.2 47 versus 84.9 35.3, p = 0.001) and there was a significant negative correlation between LVMI and coronary flow reserve. This may be due to the effect of left ventricular hypertrophy on decreasing myocardial tolerance to ischemia by creating an imbalance between oxygen supply and demand. This finding runs with those of Niizuma et al. (2008)[1] who reported that left ventricular hypertrophy (when measured by LVMI) is prevalent in HD patients (206.7 + 68.8 versus 118.6 + 33, p = 0.001) and found that CFR negatively correlated to LVMI. Also Amann et al. (1995)[12] stated that the high prevalence of LVH in ESRD population accounts for their observed excess fatal coronary heart disease events, in addition to increased coronary mass there is a reduced density of capillaries with respect to cardiomyocytes as well as an increase of the wall to lumen ratios of intramyocardial arterioles. In the same direction, Hamasaki et al. (2000)[8] studied coronary flow reserve by intravascular ultrasound examination in hypertensive subjects with normal or mildly diseased coronary arteries at angiography and demonstrated that coronary blood flow at baseline was enhanced and its response to both acetylcholine and adenosine was significantly reduced in patients with left ventricular hypertrophy suggesting that endothelium-dependent vasodilatation in hypertensive patients with LVH was impaired which is in accordance with our results. On the contrary, Tok et al. (2005)[10] reported that there was no difference in LVMI between the haemodialysis and control groups. They also found no difference in LVMI between subjects with high and low coronary flow reserve subjects, even among the haemodialysis group. Furthermore they implied that left ventricular hypertrophy is not a determinant of coronary flow reserve. Also in disagreement to our results Koivuviita et al. (2009)[11] studied by a positron emission tomography (PET)-based method whether microvascular dysfunction is an early marker of coronary dysfunction in early stages of chronic kidney disease (CKD) and found that LVMI was at the same range in both the healthy controls and the CKD patients. This is probably due to the relative short duration of dialysis in their cases since

transplantation is done rapidly.

A significant negative correlation between coronary flow reserve and duration of dialysis (r = - 0.9, p = 0.005) was found in this study which may be due to prolonged exposure to risk factors such as hypertension and dyslipidemia and left ventricular hypertrophy. This is in agreement with Goodman et al. (2000)[13] who studied coronary-artery calcification in young adults with end-stage renal disease who are undergoing dialysis found that those with calcification were older and had been undergoing dialysis for a longer period. Kandil et al. (2009)[14] found that there is no significant correlation between LVMI and duration of dialysis which does not correlate with our results and this may be due to short duration of dialysis of his studied groups.

In our study there is a highly significant negative correlation between CFR and total cholesterol, triglycerides and LDL of herodialysis patients but highly significant positive correlation with HDL and this confirm the role of dyslipidemia in progression of CAD in hemodialysis patients, this run with Caliskag et al. (2010)[2] who observed that serum cholesterol and triglyceride levels, which are known cardiovascular risk factors, were significantly higher in patients with impaired CFR. Attman and Alaupovic (1991)[15] reported that hypertriglyceridemia is most commonly observed in ESRD but has a weaker statistical association with CAD than other frequently noted lipoprotein abnormalities which contradicts with our finding and this may be due to limited number and improper dietetic control of our patients.

In our study we found significant negative correlation between CFR and blood pressure. Niizuma et al. (2008)[1] reported similar results. Also in concordance to our results, Hamasaki et al. (2000)[8] found that there was a significant impairment of CFR in patients with hypertension and left ventricular hypertrophy (LVH).

Also we found a significant positive correlation between LVMI and blood pressure. Lumpaopong et al. (2005)[16] supporting our results as he showed that systolic, diastolic blood pressures, index systolic blood pressures (ISBP), and index diastolic blood pressures (IDBP) were significantly high in LVH patients (chronic dialysis children) and blood pressure had positive correlation with left ventricular mass. On the other hand, Mitsnefes et al. (2005)[17] contradicted our results when they reported that blood pressure did not significantly correlate to LVMI.

We found no significant correlation between CFR and E/A ratio which reflects the diastolic function of studied groups with echocardiography. In contrast to our results Niizuma et al. (2008)[11] found strong inverse correlation between mitral diastolic velocities during atrial contractions and coronary flow reserve. In addition, a positive correlation was found between E/A ratio and coronary flow reserve. They concluded that decreased coronary flow reserve might contribute to the impairment of diastolic function, or vice versa. The difference between our results and Niizuma could be attributed to the relatively small sample size and the study methodology.

There was a significant negative correlation between the hemoglobin level

(r = - 0.56, p = 0.05) and the average peak coronary flow velocity at baseline. As Anemia contributes to myocardial ischemia by producing high cardiac output and increased cardiac work, reduced coronary artery filling times, reduced myocardial oxygen delivery, This correlate with Niizuma et al. (2008)A) who found the same result (r = 0.34, p = 0.02). In contrast to our result Koivuviita et al. (2009)e [11] did not observe any statistically significant correlation between hemoglobin level and basal myocardial perfusion in his study, although anaemia is one of the typical findings in CKD patients with GFR < 40 ml/min.

In our study we found significant negative correlation between CFR and C reactive protein (CRP) and this correlate with Stenvinkel and Alvestrand (2002)([18]) who reported that levels of CRP have been found to be particularly high when renal function declines to the level of ESRD.

A recent prospective study followed a cohort of more than 1000 ESRD patients for a median of 2.5 years and reported that the highest (compared with lowest) titer of CRP was associated With a 2-fold increased adjusted risk of sudden cardiac death[119)]. In agreement with our study Zimmermann et al. (1999)[(20)] also reported that CRP elevated in hemodialysis patients, in association with an atherogenic lipoprotein profile. It was also a strong predictor of death from cardiovascular events. However, Robinson et al. (2007)[(91] found no correlation between hs-CRP levels and CACS or CFR. Possibly, the lower level of inflammation and CACS in his studied patients is the result of strict exclusion criteria to eliminate the other factors that may affect CFR measurements.

We found no correlation between CFR and calcium, phosphorus, albumin and other routine parameters and this correlate with the findings of Niizuma et al., (2008)(1). Also Koivuviita et al. (2009)[(11] found that calcium phosphorus product (Ca x Pi) was higher in the CKD stage 5 group but it did not show any significant correlation with myocardial perfusion values. In contrast, Uwe Querfeld et al. (2010)[(21)] found significant associations of coronary calcifications with the following factors: Age, calcium/ phosphate product, phosphate level and PTH level.

Conclusion: CFR is significantly reduced in children with CRF on regular hemodialysis. This decrease is significantly negatively correlated with LVMI, serum level of cholesterol, LDL, triglycerides, CRP and blood pressure. So early detection and correction of these factors that significantly reduce CFR is of great concern.

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