C - Reactive Protein, Possible Valuable Predictive Inflammatory Marker in HCV Positive Hemodialysis Patients

Hesham Abouellail[1], Sameh Abdelraouf[1], Haitham Ezzat Abdelaziz[1] and Ahmed Moahmed Baha El-Dine[2]

[1]Nephrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt
[2] Internal Medicine Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt
Aha20072@yahoo.com

Abstract: The acute phase response is major pathophysiologic phenomenon that accompanies inflammation. With this reaction, normal homeostatic mechanisms are replaced by new set points that presumably contribute to defensive or adaptive capabilities. The study here included 100 subjects classified into 3 groups; the first group included 40 ESRD patients on maintenance hemodialysis with HCV positive antibody, the second group included 40 ESRD patients on maintenance hemodialysis with HCV negative antibody and the third group included 20 healthy subjects as a control group. The aim of this work is to study the response of HCV positive hemodialysis patients and its impact on CRP level as a surrogate marker of inflammation. Serum CRP level was high in both HCV positive and negative dialysis patients but it was higher in the HCV positive group so the presence of HCV may add to the state of chronic inflammation which is already present in dialysis patients.
[Hesham Abouellail, Sameh Abdelraouf, Haitham Ezzat Abdelaziz and Ahmed Mohmed Bahaa El-Dine. **C - Reactive Protein, Possible Valuable Predictive Inflammatory Marker in HCV Positive Hemodialysis Patients.** *Life Sci J* 2015;12(5):159-169]. (ISSN:1097-8135). http://www.lifesciencesite.com. 19

Key words: CRP: C reactive protein. ESRD: End stage renal disease. HCV: Hepatitis C virus. D: Hemodialysis. AVF: Arterio-venous fistula. CKD: Chronic kidney disease. SBP: Systolic blood pressure. DBP: Diastolic blood pressure. TIBC: Total iron binding capacity. TLC: Total leucocytic count. CRF: Chronic renal failure.

1. Introduction:

C-reactive protein (CRP) is a protein found in the blood, the levels of which rise in response to inflammation (i.e. C-reactive protein is an acute-phase protein). Its physiological role is to bind to phosphocholine expressed on the surface of dead or dying cells (and some types of bacteria) in order to activate the complement system via the C1Q complex ***(Thompson et al., 1999).***

CRP and other acute phase proteins are elevated in dialysis patients and cardiovascular diseases represent the single largest cause of mortality in chronic renal failure patients ***(Panichi et al., 2001).***

As CRP is so strongly associated with vascular disease, it has been suggested that this protein is not only a marker, but also a mediator, of atherogenesis. Indeed, recent in vitro data from studies on endothelial cells, monocytes-macrophages and smooth muscle cells support a direct role for CRP in atherogenesis. In ESRD, CRP has been proven to be a strong predictor of both cardiovascular and all-cause mortality, and associated with oxidative stress, vascular calcification and endothelial dysfunction ***(Stenvinkel, Lindholm, 2005).***

Hepatitis C virus (HCV) infection is a major health problem in patients with end-stage renal disease (ESRD). The incidence of acute HCV infection during maintenance dialysis is much higher than that in the general population because of the risk of nosocomial transmission. Following acute HCV infection, most patients develop chronic HCV infection, and a significant proportion develop chronic hepatitis, cirrhosis, and even hepatocellular carcinoma. Overall, chronic hepatitis C patients on hemodialysis bear an increased risk of liver-related morbidity and mortality, either during dialysis or after renal transplantation ***(Liu and Kao 2011).***

Aim of Work:

The aim of this work is to study the response of HCV positive HD patients and its impact on C-reactive protein level as a surrogate marker of inflammation.

2. Patients and Methods:

Patients:

This study was carried out at dialysis unit in Ahmed Maher teaching Hospital and dialysis unit at Ganzouri specialized hospital. The present study is a cross-sectional study that will include totally 80 adult patients and 20 control persons who will be randomly selected.

The subjects will be divided into 3 groups:

Group I: 40 patients under maintenance HD with positive HCV Ab (by ELISA).

Group II: 40 patients under maintenance HD with negative HCV Ab (by ELISA).

Group III: 20 control persons. Patients will be selected n the basis of the following inclusion and exclusion criteria:

Inclusion criteria

Chronic HD patients for at least 1 year

Exclusion criteria

- Patients with acute or chronic infectious diseases
- Patients with multi-systemic diseases
- Patients with malignancy
- Patients using AV graft or temporary catheter or infected AVF
- Previous renal transplant recipients

Methods

Patients chosen to participate in this study will be subjected to:

A. Careful history taking including age, sex, etiology of CKD, duration of dialysis of patients, dry weight, viral status and all possible forms and causes of infection.
B. Through clinical examination including body weight, BMI, blood pressure, pulse and temperature
C. Laboratory investigations

1. Complete blood cell count with differential cell count
2. Serum urea, creatinine, albumin and electrolytes
3. Lipid profile
4. ESR level
5. C-reactive protein level (with a cutoff value of 6mg/L)
6. HCV Ab by ELISA
7. Iron profile
8. Intact PTH level

3. Results:

Statistical methodology

Analysis of data was done by IBM computer using SPSS (Statistical Program for Social Science version (12) as follows:

- **Description** of quantitative variables as mean, SD and range
- **Description** of qualitative variables as number and percentage
  - **Chi-square test** was used to compare two groups as regard quantitative variable
  - **Mann Whitney test** was used instead of unpaired t-test in non-parametric data
  - **One way ANOVA test** was used to compare more than two groups as regard quantitative variable
  - **Fisher exact** test was used when one expected cell or more are less than 5.
  - **Sperman Correlation** coefficient test was used to rank different variables positively or inversely versus each other
  - **ROC** (receiver operator characteristic curve) was used to find out the best cut off and validity of certain variable.
  - Sensitivity = true ve +/true +ve + false –ve
  - = ability of the test to detect +ve cases
  - Specificity = true –ve/true –ve+ false +ve
  - = ability of the test to exclude negative cases
  - PPV (positive predictive value) = true+/true+ve +false +ve
  - = % of true +ve cases to all positive
  - NPV = true-/true-ve + false –ve
  - = % of the true –ve to all negative cases

P value > 0.05 insignificant

P> 0.05 significant

P < 0.01 highly significant

F= results of equation of ANOVA test due to name of Pearson Fisher

X^2- results of chi-square test no meaning more than this

Table (1): Comparison between the studied groups as regard general data

Variables	HCV –ve N=40	HCV +ve N=40	Controls N=20	F	*P*
Age	47.9±9	48±9	72.7±10	3.5	>0.05 NS
BMI	26.4±5	25.6±3.5	27.9±10.5	2.2	>0.05 NS
Dry weight	71.5+16	72.2±14	72.6±14	1.1	>0.05 NS
Duration	4.1+1	5.3	-	1.7#	>0.05 NS
Gender					
Male	20(50%)	20(50%)	10(50%)	0.04	>0.05 NS
Female	20(50%)	20(50%)	10(50%)		

#unpaired t-test

This table shows no statistically significant difference between the studied groups as regard general date

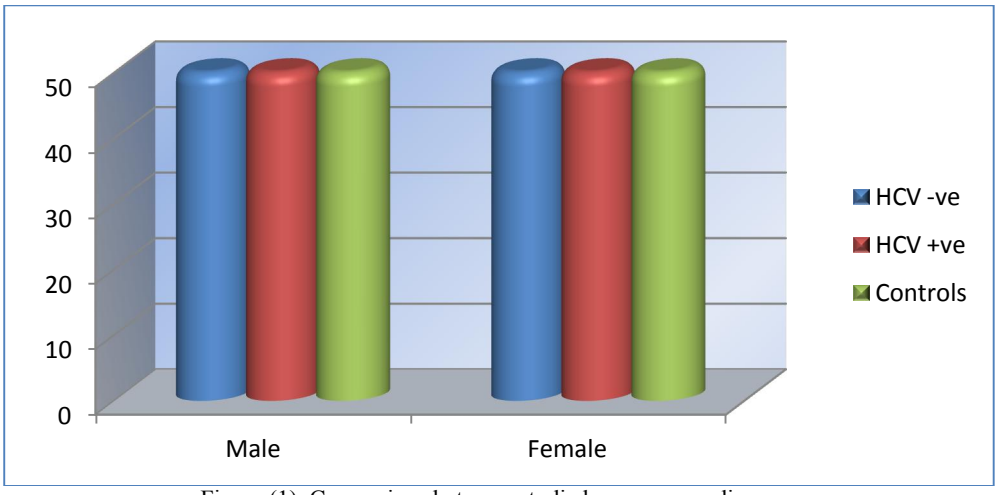
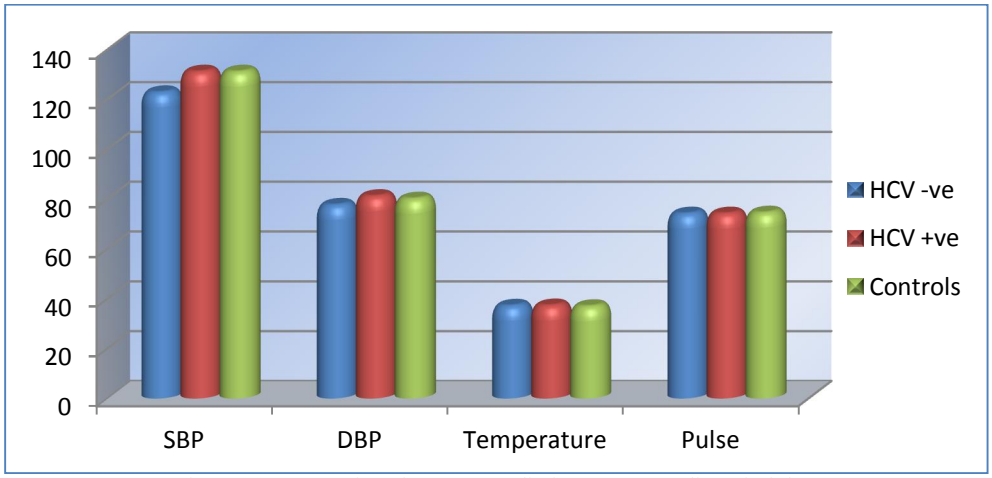


Figure (1): Comparison between studied groups regarding sex



Figure(2) :Comparison between studied groups regarding vital data

Table (2): Comparison between the studied groups as regard comorbid and vital signs

Variables	HCV –ve N=18	HCV +ve N=28	Controls	X^2	*P*
Comorbid				3.5	>0.05
1	2(11.1%)	4(14.3%)			NS
2	6(33.3%)	6(21.4%			
3	2(11.1%)	2(7.1%)			
12	2(11.1%)	4(14.3%			
22	0	0			
23	4(22.2%)	4(14.3%)			
123	1(11.1%)	6(21.4%)			
1234	0	2(7.1%)			
SBP	122.7±8	131±19	131±17	3.5#	>0.05 NS
DBP	77.5±8	81±7.5	80±6	1.8#	>0.05 NS
Temperature	37±1	37.1+1.1	36.8±1	0.4#	>0.05 NS#
Pulse	47+5.3	47±3.7	74.4±3	0.6#	>0.05 NS

 # ANOVA test

* Co-morbid: 1=DM, 2=HTN, 3=IHD, 4=CLD

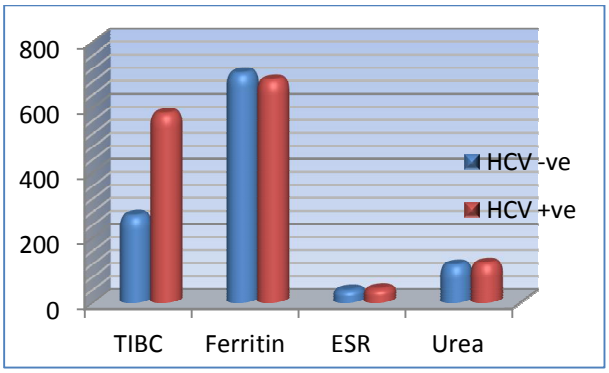
This table shows no statistically significant difference between the studied groups as comorbid and vital signs

Table (3): Comparison between the studied groups as regard lab data

Variables	HCV –ve N=40	HCV +ve N=40	Control N=20	F	*P*	LSD
PTH	431±36	581±200	42.9±13	20	<0.001 HS	1 versus 3 2 versus 3
TIBC	268±56	291±142	255±40	1.5	>0.05 NS	
Ferritin	705±336	684±300	215±58	34	<0.001 HS	1 versus 3 2 versus 3
Iron	78.2±22	73±26	96±21	6.4	<0.05 S	1 versus 3 2 versus 3
CRP	6.6+2	11.2±2.7	-	3.5	<0.001 HS#	
ESR	38.6+13	42.2±13	13.2±4	39	<0.001 HS	1 versus 3 2 versus 3
LDL	61.7±8	63.5±26	87±20	6.7	<0.001 HS	1 versus 3 2 versus 3
HDL	44.1±15	45.1±16	32.4±9	5	<0.05 S	1 versus 3 2 versus 3
TG	128+64	145±50	111±39	1.2	>0.05 NS	
Cholesterol	139.5+	141±50	140±54	2.3	>0.05 NS	
K	4.5+0.2	4.4+0.2	4.3±0.2	0.6	>0.05 NS	
Na	136±2	135.9±2	135.8±1	0.2	>0.05 NS	
Albumin	3.8±0.3	3.4+1	4.1±0.9	29	<0.001 HS	1 versus 3 2 versus 3 1 versus 2
CRP	9.6+202	8.8±1.8	0.8+0.1	165	<0.001 HS	1 versus 3 2 versus 3 1 versus 2
Urea	117+22	122+23	26.5+4.5	151	<0.001 HS	1 versus 3 2 versus 3 1 versus 2
Platelets	233+30	199±76	234±51	2	>0.05 NS	
Neutrophil	62+20	59+11	57+14	2.2	>0.05 NS	
Lymphocytes	27+10	29+4	29.9±11	0.4	>0.05 NS	
TLC	6.2+2	5.8+2	6.1+1.6	0.9	>0.05 NS	
HB	10.3+2	10.4+2	12.6+1.3	18	<0.001 HS	1 versus 3 2 versus 3

 # ANOVA test
LSD = least significant difference

This table shows statistically significant difference between the studied groups as regard different variables by using one way ANOVA test except for TIBC, ferritin, ESR, urea



Figure(3): Comparison between studied groups regarding lab data

Table (4): Correlation between CRP versus general data among HCV –ve group

Variables	CRP	
	r	*P*
Age	0.12	>0.05
BMI	0.22	>0.05
Dry weight	0.07	>0.05
Duration	0.19	>0.05
SBP	0.15	>0.05
DBP	0.22	>0.05
Pulse	0.18	>0.05

There is no significant positive correlation between CRP versus different variables by using Spearman correlation test

Table (5): Correlation between CRP versus general data among HCV +ve group

Variables	CRP	
	r	*P*
Age	-0.10	>0.05
BMI	0.11	>0.05
Dry weight	0.05	>0.05
Duration	0.12	>0.05
SBP	0.11	>0.05
DBP	0.12	>0.05
Pulse	0.23	>0.05

There is a significant positive correlation between CRP versus pulse rate no significant difference as regard other variables

Table (6): Correlation between CRP versus general data among controls

Variables	CRP	
	r	*P*
Age	-0.13	>0.05
BMI	0.10	>0.05
Dry weight	0.12	>0.05
Duration	0.19	>0.05
SBP	0.10	>0.05
DBP	0.02	>0.05
Pulse	0.21	>0.05

There is no significant positive correlation between CRP versus different variables by using Spearman correlation test.

Table (7): Correlation between CRP versus lab data among HCV –ve group

Variables	CRP	
	r	*P*
PTH	0.09	>0.05
TIBC	-0.13	>0.05
Ferritin	0.02	>0.05
Iron	0.03	>0.05
ESR	**0.69**	**<0.05S**
LDL	0.03	>0.05
HDL	-0.15	>0.05
TG	0.14	>0.05
Cholesterol	0.02	>0.05
K	**0.89**	**<0.001 HS**
Na	**0.75**	**<0.001 HS**
Albumin	0.12	>0.05
Urea	0.07	>0.05
Platelets	**-0.91**	**<0.001 HS**
Neutrophil	-0.18	>0.05
Lymphocytes	0.03	>0.05
TLC	**-0.72**	**<0.05 S**
HB	-0.19	>0.05

There is no significant positive correlation between CRP versus ESR K, and Na and inverse correlation versus platelets, TLC by using Spearman correlation test.

Table (8): Correlation between CRP versus lab data among HCV +ve group

Variables	CRP	
	R	P
PTH	**0.65**	**<0.05 S**
TIBC	-0.11	>0.05
Ferritin	0.12	>0.05
Iron	0.22	>0.05
ESR	0.19	>0.05
LDL	0.06	>0.05
HDL	-0.11	>0.05
TG	0.04	>0.05
Cholesterol	0.07	>0.05
K	0.19	>0.05
Na	0.15	>0.05
Albumin	0.10	>0.05
Urea	0.03	>0.05
Platelets	-0.11	>0.05
Neutrophil	-0.14	>0.05
Lymphocytes	0.07	>0.05
TLC	-0.12	>0.05
HB	-0.10	>0.05

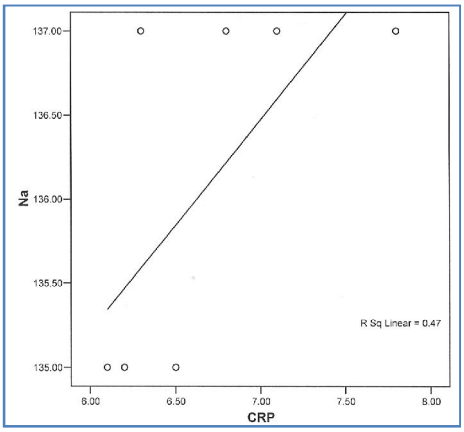


Fig.(4) : Correlation between CRP and Na

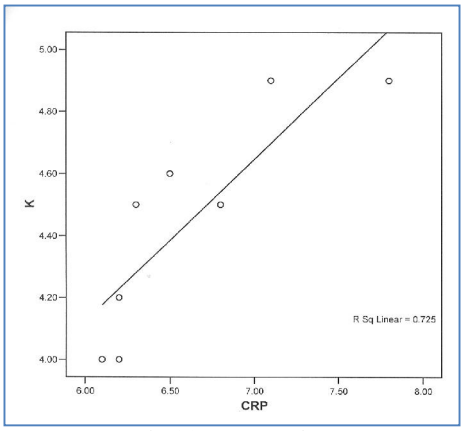


Fig.(5) : CRP and K

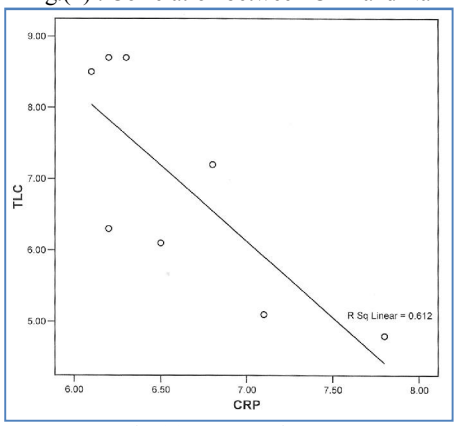


Fig.(6): CRP and TLC

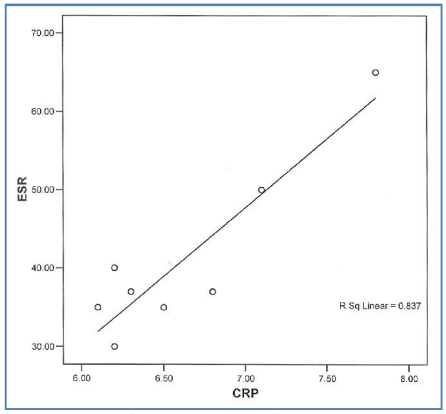


Fig.(7): CRP and ESR

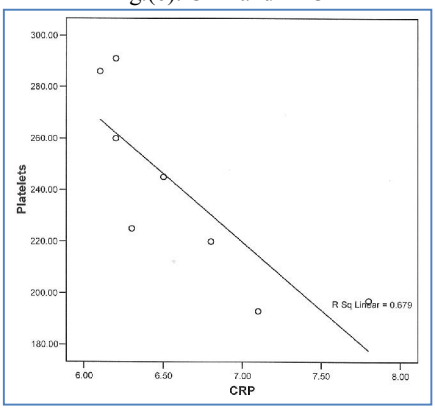


Fig.(8) : CRP and Platelets

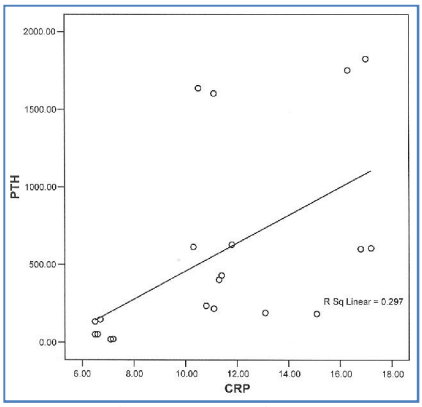


Fig.(9): CRP and PTH

There is no significant correlation between CRP versus different variables by using Spearman correlation test. There is a positive correlation versus PTH.

Table (9): Comparison between males and females as regard CRP

Variables	Gender		t	*P*
	Male	Female		
HCV –ve	6.7±0.5	6.4±0.2	1.6	>0.05 N
HCV +ve	11.9±3	8.7+2.4	1.5	>0.05 NS

There is no significant difference between males and females as regard CRP

Table (10): Validity of CRP in prediction of inflammatory changes among HCV patients

Variables	%
Best cut off value	6.5
Area under the curve (AUC)	0.90
Sensitivity	90%
Specificity	63%
PPV	70%
NPV	92%
Accuracy	75%

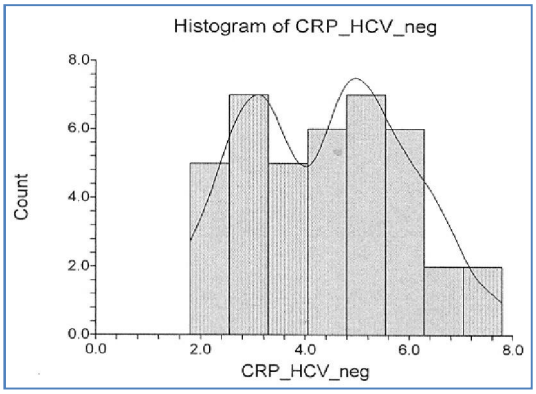
This table shows that CRP is better positive highly sensitive marker more than negative

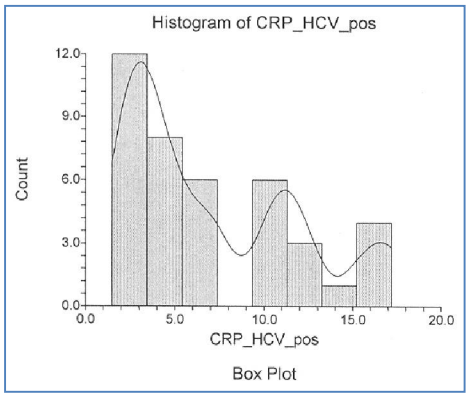
Independent t-test

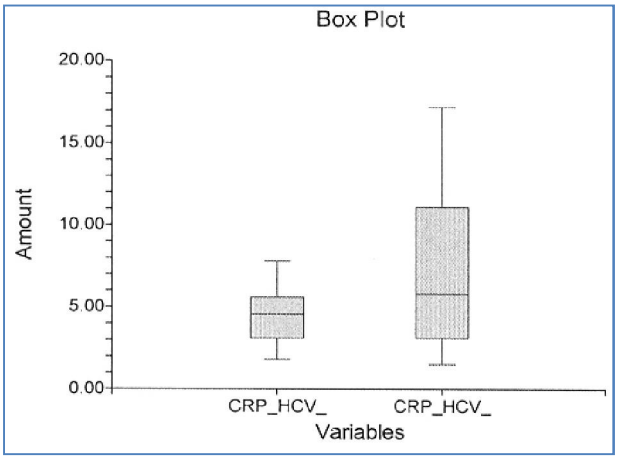
Comparing the means of CRP of HCV negative group and HCV positive group

Groups	Count	Mean	S.D	Median	p-value
HCV neg.	40	4.4225	1.554066	4.6	0.001178
HCV pos.	40	7.165	4.909778	5.85	

Plots section







Chi-square test

Comparing CRP of HCV negative group with HCV positive group

CRP	HCV negative	HCV positive	Total	Chi-square	p-value
Positive	8	20	28	7.912088	0.004911
Negative	32	20	52		
Total	40	40	80		

4. Discussion:

Recurrent or chronic inflammatory processes are common in individuals with chronic renal disease (CKD), including those with chronic renal failure (CRF) and especially end-stage renal disease (ESRD). This is due to many underlying factors, including the uremic milieu, elevated levels of circulating proinflammatory cytokines, oxidative stress, carbonyl stress, protein-energy wasting, enhanced incidence of infections (especially dialysis-access related) and others. Although the definition of inflammation is unclear in this setting, CRF-associated chronic inflammation, as assessed by increased C-reactive protein (CRP) levels above 5mg/L over at least three months, has been reported in 30 to 60 percent of North American and European dialysis patients, with dialysis patients in Asian countries possibly having a lower prevalence ***(Kalantar-Zadeh et al., 2005 and Yeun et al., 2000).***

Patients on dialysis are at a high risk for blood born infections, such as hepatitis B and hepatitis C infection. Infection with hepatitis C virus (HCV) is more common ***(Baid-Agrawal et al., 2008).***

There is a strong relationship between HCV and hemodialysis. Therefore in end-stage renal disease patients, HCV remains a significant cause of morbidity and mortality ***(Fabrizi et al., 2002).***

Hepatitis C virus (HCV) infection is an important problem in hemodialysis (HD) patients ***(Meyers et al., 2003).***

Increased morbidity and mortality in HCV-infected HD patients was shown previously ***(Stehman-Breen et al., 1998),*** and explained by a high proportion of cirrhosis and hepatocellular carcinoma of these patients ***(Espinosa et al., 2001).***

HCV infection has also been studied as a source of increased oxidative stress both in the normal and dialysis populations ***(Pawlak et al., 2004).***

Although oxidative stress is one of the possible causes of inflammation in patients with end stage renal disease ***(Kalantar-Zadeh et al., 2003),*** a greater morbidity and mortality rate with this link may be suggested in HCV infected HD patients ***(Kalantar-Zadeh et al., 2005).***

C-Reactive Protein (CRP) is one of the acute phase proteins that increase in systemic inflammation. It is produced by the liver and by fat cells ***(Nascimento et al., 2005).***

The gold standard among the microinflammatory markers in HD is C-reactive protein (CRP) ***(Yeun et al., 2000).***

Since atherosclerosis is thought to be an inflammatory disease, C-Reactive Protein (CRP), as determined by a high sensitivity immunoassay has been suggested as a strong predictor of cardiovascular risk ***(Ridker et al., 1997).***

C-reactive protein (CRP) is an independent predictor of mortality in HD patients ***(Yeun et al., 2000).*** It is easy to measure and a good predictor of short-term (1 to 2 yr) mortality and has become a routine test in HD units to warn of inflammation.

IL-6 probably is more related to mortality and is associated with more causes of inflammation than CRP ***(Panichi et al., 2004)*** however, it is more difficult to measure, and it is of little use in clinical practice.

CRP is produced under the control of various pro-inflammatory cytokines such as interleukin 1 (IL-1), IL-6 and tumor necrosis factor α (TNF-α) ***(Arici and Walls 2001).***

IL-6 is the prototypic pleiotropic cytokine commonly produced at local tissue sites, and circulating receptors modulate the biological effects of cytokines ***(Paysant et al., 2000).***

Hepatitis C (HCV) is not an uncommon feature in hemodialysis (HD) patients and may be a cause of systemic inflammation. Plasma cytokine interleukin-6 (IL-6) is mainly produced by circulating and peripheral cells and induces the hepatic synthesis of C-reactive protein (CRP), which is the main acute phase reactant. The aim of this study was to investigate the influence of HCV on serum CRP as a marker of systemic inflammation, in H patients.

This study was conducted on 100 person divided to 3 groups:

Group I: 40 patients under maintenance HD with positive HCV Ab (by ELISA).

Group II: 40 patients under maintenance HD with negative HCV Ab (by ELISA).

Group III: 20 control persons

This study showed no statistically significant difference between the studied groups regarding general data, comorbid conditions and vital signs.

Concerning the laboratory data we did find a significant difference in serum albumin level in the control group compared to the other two groups (dialysis groups) as the mean serum albumin level in the control group was (4.1±0.9) while in the HCV negative dialysis group it was (3.8±0.3) and in HCV positive dialysis group it was (3.4+1).

This finding shows one of the main problems we face with ESRD patients which is malnutrition. Malnutrition is associated with cardiac co-morbidity, inflammation and poor survival in ESRD patients.

Consistent with this study there was a study done in Department of Clinical Laboratory Sciences, School of Allied Medical Sciences, Tehran University of medical Sciences, Tehran, Iran on 300 hemodialysis patients by ***(Nasrin et al., 2012)*** which showed that mean serum albumin was 4.07 g/dl (±0.19) of 300 patients, 21 died (7%). These were patients with serum albumin <4 g/dL.

Also the present study showed that the CRP level in dialysis patients (both positive and negative) was much higher than the control group as it was (8-9) denoting the condition of chronic inflammation in dialysis patients.

Consistent with this study there was a study done in Department of Clinical Laboratory Sciences, School of Allied Medical Sciences, Tehran University of medical Sciences, Tehran, Iran on 300 hemodialysis patients by ***(Nasrin et al., 2012)*** which showed that mean serum CRP was 7.96 mg/dL (±1.52).

Greater CRP levels indicate patients at risk of progression of cardiovascular disease ***(Harris et al., 1999).*** The presence of elevated CRP in a significant number of ESRD patients confirms the existence of chronically activated APR.

Recent data from ESRD patients also showed elevated CRP levels have significant association with hypoalbuminemia, malnutrition increased morbidity and mortality in ESRD patients ***(Arici and Walls 2001).***

Also the present study showed a significant difference between the studied groups concerning Hb level as the mean level in the control group was higher than both dialysis groups.

Factors likely contributing to anemia in ESRD include blood loss, shortened red cell life span, vitamin deficiencies, the "uremic millieum," erythropoietin (EPO) deficiency, iron deficiency, and inflammation.

The present study showed no significant difference in CRP level between males and females. But it showed a very significant difference when we compared the HCV positive group with HCV negative one as in the HCV positive group 20 of the 40 examined patients (50%) their CRP level was positive while only 8 patients (20%) in the HCV negative group came with a positive CRP level.

When comparing the means of CRP of HCV negative group and HCV positive group we get a p-value of (0.001178) by using independent t-test.

While when comparing CRP of HCV negative group with HCV positive group we get a p-value of (0.004911) using the Chi-square test.

Also our study showed that the best cut off value of CRP is about 6.5 mg/dL with a sensitivity of 90%, specificity of 63% and accuracy of 75% so CRP is considered (in our study) as very good sensitive marker better than specific.

Consistent with our study done by ***(Nadeem et al., 2011)*** in Pakistan a total of 43 patients (39.5% men and 60.5% women; age range, 21 to 65 years) on maintenance hemodialysis for a period of at least 3 months were included. Twenty-four of them were HCV positive. Serum CRP and IL-6 were assessed in all patients and they found high serum IL-6 and CRP levels in HCV-positive hemodialysis patients, compared with HCV-negative ones.

Also consistent with our study there was a study done by ***(Tuncer et al., 2011)*** where a total of 84 patients with clinically suspected hepatitis C were included in this study, in which anti-HCV was detected to be positive. Eighty four anti HCV positive samples were divided into two groups according to the HCV RNA results, as the HCV RNA positive group (Group 1, 50 samples) and the HCV RNA negative group (Group 2, 34 samples) and they found that 50 of the 84 samples with anti HCV positivity were detected to be positive for HCV RNA (Group 1), whereas 30 were detected as negative (Group 2). While the hsCRP values were found to be above the normal level in 11 (22%) of the 50 area samples in the first group, and in 3 (8.8%) of the 34 sera samples in the second group.

In disagreement with our study there was a study done by ***(Nascimento et al., 2005)*** in Brazil and included 118 HD patients (47% males, age 47±13 years) who had been treated by standard HD for at least 6 months. The patients were dividedinto two groups depending on the presence (HCV+) or absence (HCV-) of serum antibodies against HCV.

They found that the median level of serum hsCRP (mg/1) was lower in the HCV+ group than in the HCV- group, but this difference was not statistically significant (P = 0.08).

So our study showed that CRP is a good predictive inflammatory marker in ESRD patients in both dialysis groups (compared to the control group) and it was higher in the HCV positive group than in the HCV negative one.

Summary:

Recurrent inflammatory processes are common in individuals with chronic renal disease (CKD), including those with chronic renal failure (CRF0 and especially end-stage renal disease (ESRD). This is due to many underlying factors, including the uremicmilieu, elevated levels of circulating proinflammatory cytokines, oxidative stress, carbonyl stress, protein-energy wasting, enhanced incidence of infections (especially dialysis-access related) and other. Although the definition of inflammation is unclear in this setting, CRF-associated chronic inflammation, as assessed by increased C-reactive protein (CRP0 levels above 5 mg/L over at least three months, has been reported in 30 to 60 percent of North American and European dialysis patients, with dialysis patients in Asian countries possibly having a lower prevalence.

The acute phase response is major pathophysiologic phenomenon that accompanies inflammation. With this reaction, normal homeostatic

mechanisms are replaced by new set points that presumably contribute to defensive or adaptive capabilities.

Acute phase proteins are defined as those proteins whose plasma concentrations increase (positive acute phase proteins), such as C-reactive protein (CRP), or decrease (negative acute phase proteins) such as albumin, during inflammatory states.

Measurement of the levels of these proteins is frequently utilized to define the presence and/or degree of inflammation in a given patient. A number of inflammatory markers have been studied in patients with CKD.

Despite its name, the "acute" phase response can persist over months to years and become chronic. In such states of chronic inflammation, positive acute phase proteins including CRP(normal range <1 mg/L) may be slightly but persistently increased, which can predispose to an increased risk of atherosclerotic cardiovascular disease (CRP 1 to 3 mg/L). However, in many CKD patients, especially in maintenance dialysis patients, serum CRP levels are persistently between 5 and 50 mg/dL, although they may fluctuate widely.

The study here included 100 subjects classified into 3 groups; the first group included 40 ESRD patients on maintenance hemodialysis with HCV positive antibody, the second group included 40 ESRD patients on maintenance hemodialysis with HCV negative antibody and the third group included 20 healthy subjects as a control group.

The aim of this work is to study the response of HCV positive hemodialysis patients and its impact on CRP level as a surrogate marker of inflammation.

The patients were chosen on the basis of being on maintenance hemodialysis for at least one year and we excluded patients with acute or chronic infectious disease, with multi-systemic diseases, with malignancy, using AV graft or temporary catheter or infected AVF and previous renal transplant recipients.

The patients were subjected to careful history taking including age, sex, etiology of CKD, duration of dialysis of patients, viral status and all possible forms and causes of infection plus thorough clinical examination including body weight, BMI, blood pressure, pulse and temperature.

Both patients and normal subjects were subjected to laboratory investigations that included complete blood cell count with differential cell count, serum urea, cratinine, albumin and electrolytes, lipid profile, ESR level, C-reactive protein level (with a cutoff value of 6 mg/L), HCV Ab by ELISA and iron profile.

In the study we found a significant difference in serum albumin level between the control group and the dialysis groups as it was much higher in the control group which confirms the fact of malnutrition in ESRD patients.

Also the present study showed a significant difference between the studied groups concerning Hb level as the mean level in the control group was higher than both dialysis groups.

The study also showed that serum CRP level was much higher in the dialysis groups than the control group denoting the condition of chronic inflammation in ESRD patients.

The present study showed no significant difference in CRP level between males and females. But it showed a very significant difference when we compared the HCV positive group 20 of the 40 examined patients (50%) their CRP level was positive while only 8 patients (20%) in the HCV negative group came with a positive CRP level.

When comparing the means of CRP of HCV negative group and HCV positive group we get a p-value of (0.001178) by using independent t-test.

While when comparing CRP of HCV negative group with HCV positive group we get a p-value of (0.004911) using the Chi-square test.

Also our study showed that the best cut off value of CRP is about 6.5 mg/dL with a sensitivity of 90% specificity of 63% and accuracy of 75% so CRP is considered (in our study) as very good sensitive marker better than specific.

Systemic inflammatory marker CRP also has been shown to play an important role in promotion of atherothrombosis by increasing recruitment of monocytes (Ma, 2007).

Conclusion:

From the present study, it is possible to conclude that:

- Serum hemoglobin and albumin levels are lower in ESRD than normal population denoting the state of malnutrition in those patients
- Serum CRP level is much higher in dialysis patients than in normal population denoting the state of chronic inflammation in those patients
- The best cut off value of CRP is about 6.5 mg/dL with a sensitivity of 90%, specificity of 63% and accuracy of 75% so CRP is considered as very good sensitive marker better than specific.
- Serum CRP level was high in both HCV positive and negative dialysis patients but it was higher in the HCV positive group so the presence of HCV may add to the state of chronic inflammation which is already present in dialysis patients.

References:

1. Arici M & Walls J (2001): End-stage renal disease, atherosclerosis, and cardiovascular mortality, is C-

reactive protein the missing link? Kidney international, 59: 407-414.
2. Baid-Agrawal S,Pascual M, Moradpour D, *et al.* (2008): Hepatitis C virus infection in haemodialysis and kidney transplant patients, Rev Med Virol; 18:97-115.
3. Espinosa M, martin-Malo A, Alvarez de Lara MA, *et al.* (2001): Risk of death and liver cirrhosis in anti-HCV-positive long-term hemodialysis patients. Nephrol Dial Transplant; 16: 1669-1674.
4. Fabrizi F, Poordad FF, Martin P (2002): Hepatitis C infection and the patient with end-stage renal disease. Hepatology; 36: 3-10.
5. Harris TB, Ferrucci L, Tracy RP, Corti MC, *et al.* (1999): Associations of elevated interleukin-6 and C-reactive protein levels with mortality in the elderly. American Journal of Medicine; 106: 506-512.
6. Kalantar-Zadeh (2005): Recent advances in understanding the malnutrition-inflammation-cachexia syndrome in chronic kidney disease patients: What is next? Semin Dial; 18: 365.
7. Kalantar-Zadeh K, Ikizler A, Block G, *et al.* (2003): Malnutrition-inflammation complex syndrome in dialysis patients, causes and consequences; Am J Kidney Dis; 42: 864-881.
8. Kalantar-Zadeh K, McAllister CJ, *et al.* (2005): Clinical characteristics and mortality in hepatitis C-positive hemodialysis patients, a population based study. Nephrol Dial Transplant; 20: 1662-1669.
9. Liu CH, Kao JH (2011): Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan. kaojh@ntu.edu.tw.j. Gastroenterol Hepatolerosclerosis. Circulation; (103): 1194-1197.
10. M. Clinton Miller, Ph.D., Rebecca G. Knapp: Clinical epidemiology and biostatistics, published by Williams & Wilkins, Maryland: 3rd edition 1992.
11. Ma Hongbao, Relationship of Inflammation/Thrombosis and C-reactive protein (CRP), Plasminogen Activator Inhibitor 1 (PAI-1), Inteleukin-6 (IL-6), Inteleukin-1 (IL-1), Tissue Factor (TF), Tumor Necrosis Factor-alpha (TNF-α), tTssue Plasminogen Activator (tPA), CD40. Nature and Science. 2007;5(4):61-74.
12. Meyers CM, Seeff LB, Stehman-Breen CO, Hoofnagle JH (2003): Hepatitis C and renal disease, an update. Am J Kidney Dis; 42: 631-657.
13. NadeemAfzal, Sarwar Abbas, Azazmand Ahmed, *et al.* (2011): Effect of hepatitis C virus on C-Reactive protein and interleukin-6 in hemodialysis patients; IJKD 5: 182-6.
14. Nascimento MM, BruchfeldA, Suliman ME, *et al.* (2005): Effect of hepatitis C serology on C-reactive protein in a cohort of Brazilian hemodialysis patients; Braz J Med Biol Res; 38(5).
15. Nasrin Dashtil, Nahid Einollahil, Fariba D, *et al.* (2012): ActaMedicaIranica; 50(3): 197-202.
16. Panichi V, Maggiore U, Taccola D, *et al.* (2004): Interleukin-6 is a stroner predictor of total and cardiovascular mortality than C-reactive proteinindialytic patients. Nephrol Dial Transplant; 19: 1154-1160.
17. Panichi V, Migliori M, and De Pietro S, *et al.* (2001): Department of Internal Medicine of Pisa, university of Pisa, Italy. V.panichi@int.med.unipi.it. Ren Fail. May-Jul; 23(3-4): 551-62.
18. Pawlak K, Pawlak D, Mysliwiec M (2004): Hepatitis intensified oxidative stress, MIP-1 beta and RANTES plasma levels in uremic patients. Cytokine; 28:197-204.
19. Paysant J, Blanque R, Vasse M, Soria C *et al.* (2000): Factors influencing the effect of the soluble IL-6 receptor on IL-6 responses in HepG2 hepatocytes, Cytokine; 12: 774-779.
20. Ridker PM, Cushman M, Stampfer MJ, *et al.* (1997): Inflammation, aspirin, and the risk of cardiovascular disease in apparently healthy men. The new England Journal of medicine; vol. 336: No. 14 pp. 973-999.
21. Stehman-Breen CO, Emerson S, Gretch D, Johnson RJ (1998): Risk of death among chronic dialysis patients infected with hepatitis C virus. Am J Kidney Dis; 32:629-634.
22. Stenvinkel P, Linddholm B (2005): Division of renal medicine and baxternovum. Department of clinical science, Karolinska University. 23(1): 27-8.
23. Thompson DM, Pepys MB, Wood SP(1999): The physiological structure of human C-reactive protein and its complex with phsophocholine. Structure 7(2): 169-77.
24. Tuncer Ozekinci, Selahattin Atamca, Hasan Akbayin (2011): Correlation of high sensitive C-reactive protein and Hepatitis C virus RNA in anti-HCV-positive sera doi; 10.5798/diclemedj. 0921.2011.02.0002.
25. Yeun JY, Levine RA, mantadilok V, Kaysen GA (2000): C-reactive protein predicts all-cause and cardiovascular mortality in hemodialysis patients. Am J Kidney Dis 35: 469-476.

5/16/2015