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Effect of Endotoxemia on Cardiac Disease in High & Low Flux Hemodialysis Patients

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ABSTRACT

Background : endotoxemia can be the missing link between ESRD and cardiac disease , the first cause of death in hemodialysis patients .

Patients and methods : patients were recruited from Ain Shams University Hospitals , hemodialysis units .120 patients on prevalent HD were enrolled in the study : 31 cardiac patients on high flux HD (group A) , 29 cardiac patients on low flux HD (group B), 32 non – cardiac high flux HD (group C), and 28 non – cardiac low flux HD (group D) . For all patients we measured : Hb , URR , serum albumin , HsCRP, predialysis and postdialysisa endotoxin , endotoxin delta change, echocardiography , and ECG . **Results :** we found that cardiac high flux and low flux groups had higher endotoxemia levels than non – cardiac high flux and low flux groups .**Conclusion :** High flux hemodialysis patients had higher accumulated endotoxin than low flux hemodialysis patients, within either cardiac or non - cardiac groups .

Keywords : Endotoxemia - Hemodialysis - Cardiac disease - High & low flux dialysis .

INTRODUCTION

Bacterial endotoxin is a lipopolysaccharide (LPS) which represents the major glycolipid component of the outer membrane of gram – negative bacteria and accounts for 70 % of the total bacteria in the healthy human gut .Translocated endotoxin derived from intestinal bacteria has a wide range of adverse effects on cardiovascular (CV) structure and function , driving systemic inflammation , atherosclerosis , and oxidative stress .[1] Also , it results in peripheral vasodilation and reduction in cardiac contractile performance .[2]

Chronic kidney disease patients are characteristically exposed to significant endotoxemia . In particular , hemodialysis induced systemic circulatory stress and recurrent regional ischemia may lead to increased endotoxin translocation from the gut . This represents a crucial missing link in understanding the pathophysiology of the grossly elevated CV disease risk in CKD patients .[3]

The precise mechanism by which HD aggravates endotoxemia in ESRD patients remains unknown .[4]

Volume overload and fluid retention being highly prevalent in HD patients , contributes in generalized and bowel edema which impairs intestinal epithelial barrier function .[5]

The reported degree and prevalence of endotoxemia in HD patients varies in the literature . May be the varied findings are due to difficulties in the accurate detection of endotoxin in blood with the limulus amebocyte lysate assay (LAL assay) , the most extensively used method in blood endotoxin detection .[6]

High serum LPS activity is strongly associated with the components of the metabolic syndrome .[7]

PATIENTS AND METHODS

Our study was conducted on 120 patients on prevalent hemodialysis.Patients were recruited from Ain Shams Hemodialysis Hospitals ,hemodialysis units. All patients were on prevalent hemodialysis , having 3 sessions / week , 4 hours / session , and were using bicarbonate containing dialysate .Net fluid removal , blood pump speed , and Heparin dose were set on an individual basis according to clinical findings .

Patients included in the study were divided into 4 groups as follows : Group A included 31 hemodialysis cardiac patients (patients having a previous and current positive cardiac disease), dialyzed with high flux dialyzer , while Group B included 29 hemodialysis cardiac patients dialyzed with low flux dialyzer . Group C comprised 32 non-cardiac hemodialysis patients

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dialyzed with high flux dialyzer , while Group D comprised 28 non – cardiac hemodialysis patients dialyzed with low flux dialyzer .

We excluded from the study patients under 18 years old , those having active infections , active autoimmune disease , diabetic patients , those having malignancy , patients dialyzed from central venous catheter , and patients having serum calcium , serum phosphorus , Calcium – Phosphorus product above or below KDIGO guidelines & also serum PTH being above or below KDIGO guidelines , in order to eliminate their effect on functional cardiac disease .

We obtained an informed consent from all patients enrolled in the study .

The following data were obtained from all patients :complete medical history including : age (years) , sex , dry weight (Kg) , body mass index (BMI , Kg / m^2) , duration of hemodialysis (months) , predialysis systolic and diastolic blood pressure (mm Hg) , ultrafiltration rate (UFR , ml /h) , and blood pump speed .

Fasting blood samples were collected before the mid – week hemodialysis session (before Heparin administration) , for all biochemical tests performed with the exception of postdialysis urea level and postdialysis serum endotoxin level .

For all patients , we performed the following laboratory tests according to conventional methods used within Clinical Pathology department , Ain Shams University Hospitals , Cairo , Egypt : Hb level (g / dl) , urea reduction ratio (URR , in %) , serum albumin (g/ dl) , highly sensitive CRP (Hs CRP) (mg / dl) , endotoxin blood level (lipopolysaccharide) : predialysis endotoxin level (pre Endo. , Eu / ml) , postdialysis endotoxin level (post Endo , Eu / ml) , and delta change of endotoxin (delta change between predialysis and postdialysis levels) .

$$URR = \frac{U\ pre - U\ post}{U\ pre} \times 100\%$$

Endotoxin level measurement : predialysis and postdialysis serum samples were obtained to measure endotoxin levels of both .In addition , delta change of endotoxin level was calculated as :

Delta change of endotoxin = (predialysis endotoxin) – (postdialysis endotoxin) .

Serum endotoxin level quantification in (Eu / ml) , was done using an ELISA Kit (Glory Science Co. , Ltd. , USA , Catalog # : A 1093) , with a detection range of : 0.02 Eu / ml - 0.8 Eu / ml .[8]

Electrocardiographic and echocardiographic (e D) Assessments were performed for all patients to assess presence or absence of cardiovascular disease . The following measurements were performed :

- Left ventricular ejection fraction (EF) .

EF = Stroke volume / End diastolic volume

EF > 75 % → Hyperdynamic circulation

EF : 55 % - 74.9 % → Normal

EF : 40 % - 54.9 % → Mildly reduced function

EF : 30 % - 39.9 % → Moderately reduced function

EF < 30 % → Severely reduced function

- Left ventricular hypertrophy (LVH) was detected through performing an ECG : S in V_1 + R in $V_6 \geq 35$ mm OR R in a VL $\geq$11 mm . Also LVH can be confirmed by the ECHO (if left ventricular wall thickness > 11 mm) /

- Atrial fibrillation (AF) : was confirmed by absence of P wave in ECG together with an irregular ventricular rhythm .

-Ischemic heart disease (IHD) : was confirmed through detecting present or past ischemic changes in ECG : ST segment elevation ,Pathological Q wave , and Inverted T wave . Echocardiographically detected cardiac ischemic changes : Segmental wall motion abnormalities , and hypokinetic myocardium.

- Echocardiographically detected pericardial effusion .

Statistical analysis

Data were collected , coded , revised , and entered to the Statistical Package for Social Science (IBM SPSS) version 21 .Data were represented as mean , standard deviations , and ranges for the quantitative data with parametric distribution while median interquartile ranges for the quantitative data

with non-parametric distribution and number with percentages for the qualitative data .

The comparison between groups with qualitative data were performed by using Chi – square test or Fischer exact test .

The comparison between two independent groups with quantitative data and parametric distribution were performed by using Independent t – test while non – parametric distribution data were compared using Mann – Whitney test .

Spearman correlation coefficients were used to assess the relation between two quantitative parameters .

Logistic regression analysis were to assess the significant items between groups with their Odds Ratio . Linear regression analysis was used to assess the significant items affecting endotoxin .

P – value was considered as follows :

P > 0.05 : Non – significant

P < 0.05 : Significant

P < 0.01 : Highly significant

RESULTS

In our study , age showed a mean value of 55.19 ± 10.75 years in cardiac high flux HD patients of Group A , a mean value of 58.83 ± 10.30 years in cardiac low flux HD patients of Group B , a mean value of 44.56 ± 14.44 years in non – cardiac high flux HD patients of Group C , and a mean value of 51.46 ± 12.01 years in non – cardiac low flux HD patients of Group D .

Group A comprised 7 female patients (22.6 %) and 24 male patients (77.4 %) , while Group B included 12 female patients (41.4 %) and 17 male patients (58.6 %) . Group C comprised 20 female patients (62.5 %) and 12 male patients (37.5 %) , while Group D included 7 female patients (25 %) and 21 male patients (75 %) .

Dry weight mean value was 77.03 ± 17.95 Kg in group A , 74.52 ± 14.95 Kg in group B, 63.34 ±26.69 Kg in group C , and 73.18 ± 15.85 Kg in group D .

BMI mean value was 25.16 ± 4.48 Kg / m^2 in group A , 25.52 ± 4.04 Kg / m^2 in group B , 23.53 ± 6.76 Kg / m^2 in group C , and 25.61 ± 5.43 Kg / m^2 in group D .

Duration of HD median value was 84 ms (ranging from 8 – 264) in group A , 72 ms (ranging from 8 – 240) in group B , 84 ms (ranging from 8 – 360) in group C , 102 ms (ranging from 8 – 240) group D .

Pump Speed mean value was 306.45 ± 33.52 ml / min in group A , 259.48 ± 33.12 ml / min in group B , 288.28 ± 34.19 ml / min in group C , 289.29 ± 28.41 ml/min (ranging from 250 – 350) in group D.

Ultrafiltration rate (UF) median value was 600 ml / h (ranging from 100 – 1100) in cardiac high flux HD patients (group A) , 750 ml / h (ranging from 250 – 1100) in cardiac low flux HD patients (group B) , 500 ml / h (ranging from 100 – 1000) in non – cardiac high flux HD patients (group C) , and 500 ml / h (ranging from 125 – 1000) in non – cardiac low flux HD patients (group D) .

Predialysis systolic BP mean value was 123.23 ± 19.22 mmHg in group A , 125 ± 19.93 mmHg in group B , 126.88 ± 16.93 mmHg in group C , 126.43 ± 22.97 mmHg in group D .

Predialysis diastolic BP mean value was 76.45 ± 12.53 mmHg in group A , 77.93 ± 10.82 mmHg in group B , 77.50 ± 9.84 mmHg in group C , 75.71 ± 13.99 mmHg in group D .

Urea reduction ratio % mean value 66.39 ± 10.98 within group A , 50.00 ± 23.00 within group B , 64.88 ± 11.01 within group C , and 59.61 ± 12.03 within group D .

Serum albumin mean value was 3.93 ± 0.57 gm / dl within group A , 4.00 ±0.80 gm / dl within group B , 3.99 ± 0.50 gm / dl within group C , and 3.91 ± 0.62 gm / dl within group D .

Hb mean value was 10.28 ± 1.78 gm / dl within group A , 10.04 ± 1.68 gm / dl within group B , 9.83 ± 1.80 gm / dl within group C , and 9.34 ± 1.38 gm / dl within group D .

Hs CRP mean value was 70.59 ± 15.15 mg / L within group A , 73.77 ± 17.31 mg / L within group B , 65.74 ± 28.56 mg / L within group C , and 81.11 ± 22.44 mg / L within group D .

DISCUSSION

Since in healthy humans , the epithelial barrier prevents translocation of bacteria and their harmful products and components , the presence of endotoxemia and the detection of

the gut microbial DNA in the blood of end stage renal disease patients , points to impairement of intestinal barrier structure and function .[9]

In vitro studies revealed significant depletion of the tight junction proteins , and reduction of the trans – epithelial electric resistance (TER) in cultured human colonocytes incubated in media containing human uremic plasma .[10]

In addition to disrupting the epithelial barrier , advanced chronic kidney disease alters the composition and function of the intestinal microbiome .[11]

Endotoxin contamination of dialysis water has long been recognized as a cause of CV instability during dialysis . Serum endotoxin levels were nearly 6 times higher in chronic kidney disease patients receiving dialysis compared with who were not yet on dialysis .[3]

Since cardiac cells express Toll – like receptor 4 (TLR4) , the heart is a target for endotoxemia . Sustained activation of the innate immune system in the heart by TLR4 may have diverse adverse myocardial effects .[12] This may explain in part the markedly increased cardiovascular death rate in HD patients .[13]

The reported mean concentration of serum endotoxin level in healthy individuals using limulus amebocyte lysate (LAL) assay was 0.128 EU / ml .[14]

We considered Endotoxin alert level (= 0.125 EU / ml) and Endotoxin standard level (= 0.250 EU / ml) , according to the study conducted by *Griet et al.*[15]

Predialysis endotoxin mean levels were just above standard level for Endotoxin , within cardiac high & low flux groups , and also non – cardiac high & low flux groups , with non – significant difference on comparing different groups together . An highly significant correlation existed in our study between predialysis endotoxin level and URR % within cardiac high flux group A , having the highest percentage of patients having decreased endotoxin wash out . This could be the effect of the association of cardiac affection by endotoxemia together with the high flux hemodynamic HD procedure encouraging gut leak .

Mcintyre *et al.*[3] , have reported that , in their study , 41 out of 66 of established HD patients studied exhibited significant levels of dialysis induced myocardial stunning , and that predialysis endotoxin level showed a significant correlation with : myocardial stunning severity (r = 0.44 , P = 0.035) , predialysis serum cardiac troponin T (cTnT), and increased risk of mortality . In our study , this correlation did not exist , but in each of cardiac low flux group B & non - cardiac high flux group C ,(both having a better endotoxin wash out than group A) ,predialysis endotoxemia was inversely correlated to pump speed (r = - 0.441 , P = 0.017 & r = - 0.388 , P = 0.028 , respectively) .

Postdialysis endotoxin mean levels were higher in non – cardiac high & low flux groups than cardiac high and low flux groups in a non – signifoicant way , which is against what was expected for endotoxin as being a causative agent as well as an effect of combined compromised tissue perfusion & uremic state for cardiac patients on hemodialysis . We also found that postdialysis endotoxin mean levels were lower in cardiac high flux group A than cardiac low flux group B , and similarly we had a lower postdialysis endotoxin level in non - cardiac high flux group C than in non – cardiac low flux group D , in a non – significant way . This was possibly due to better endotoxin wash out by high flux dialysis . This doesn ' t agree with the theory of back diffiusion of bacterial endotoxin from dialysate into patient ‘ s blood during hemodialysis procedure . Also , this is against the theory that there is more hemodynamic instability associated with high flux dialysis , with more regional ischemia , and more gut microbiota translocation .?

McIntyre et al.[3], in their study reported that post – HD circulating endotoxin levels were significantly correlated with fluid removal (UF volume) .This relationship didn ‘ t exist in our study .

Henrie et al.[16] , reported that high – flux dialysis membranes used with bicarbonate dialysis fluid increase the risk of back diffusion of bacterial endotoxin into the blood during hemodialysis .?

Our deductions were confirmed by finding a nearly fixed proportion of patients (around 30 %) , having a constant pre - and post – dialysis endotoxin levels (Endotoxin delta change = zero) within cardiac high flux group A and non – cardiac high & low flux groups C & D , except for cardiac low flux group B which had the highest percentage of patients (55 %) having fixed pre - & post – dialysis endotoxin levels , (the highest proportion of lack of endotoxin wash out) , in a statistically non – significant way .

Non – cardiac high flux group C & non – cardiac low flux group D had the highest percentages of patients showing increase in Endotoxin delta change , which could mean that washing out of endotoxin has protected those patients from being cardiac , inspite of being uremic and on regular hemodialysis , without a solid statistical evidence . This was confirmed by having the highest percentages of patients having a decrease of Endotoxin delta change (which means a decrease in Endotoxin wash out) in cardiac high flux group A followed by cardiac low flux group B , in a statistically non – significant way .

On adding percentages of patients having Endotoxin Zero delta change to percentages of patients having Endotoxin decrease in delta change (both types of patients having decreased wash out of endotoxin) , in the four studied groups , we found that accumulation of endotoxin was the highest within cardiac high flux group A (77.4 %) & cardiac low flux group B (72.4 %) , followed by non – cardiac high flux group C (67.9 %) , and it was the least in non – cardiac low flux group D (56.2 %). This was up to a certain extent an indirect evidence of Endotoxin – cardiac disease relationship , within uremic patients on hemodialysis . Also , existence of higher level of accumulated endotoxin in high flux than low flux dialysis patients , among cardiac and non – cardiac groups as being observed separately , agrees to some extent with the bacterial endotoxin back diffusion theory . More extended studies including large numbers of patients are still required to prove this relationship .

Mcintyre et al.[3] , reported that circulating endotoxemia was most notable in those with the highest CV disease burden , and a sharp increase was observed after initiation of hemodialysis .

Ejection fraction (EF) was higher in cardiac low flux group B as compared to cardiac high flux group A (having the higher percentage of patients with endotoxin accumulation) , (P = 0.057) . This relationship didn ' t exist between non – cardiac high & low flux group C & D as they both had the lower percentages of patients with endotoxin accumulation , and they both also had the highest percentages of patients having ejection fraction category of 55 – 75 % . Non – cardiac high flux group C (having more than 65% of its patients with accumulated endotoxin) showed a much higher ejection fraction than does cardiac high flux group A (having the highest percentage of patients with accumulated endotoxemia) , (P = 0.000 , table 3) & this is another indirect proof of our previous deductions concerning endotoxemia – cardiac disease relationship . This relationship was confirmed by a highly significant Odds Ratio (Sig = 0.001 , OR = 0.889 , 95 % Confidence Interval CI = 0.837 – 0.946) . Also , non – cardiac low flux group D (having the least percentage of patients with accumulated endotoxemia) had a significantly higher EF than cardiac low flux group B (P = 0.009 , table 4) . This was also confirmed by a highly significant Odds Ratio (Sig = 0.016 , OR = 0.917 , 95 % CI = 0.855 – 0.984) .

Kumar et al.[2] , reported that , in their study , there was a significant correlation between severity of HD – induced cardiac stunning and endotoxin level , and this agrees with our findings .

On the contrary , *McIntyre et al.*[3] stated that in their hemodialysis patients who underwent echocardiography , left ventricular ejection fraction was relatively well preserved .

Percentage of patients having left ventricular hypertrophy as a marker of cardiac dysfunction was higher in non – cardiac low flux group D (having higher male percentage & least percentage of patients having accumulated endotoxemia) than in non – cardiac high flux group C (having higher female percentage & more than 65 % of its patients with accumulated endotoxemia), (P = 0.041) .This

situation didn ‘ t exist on comparing other groups , which could mean that LVH didn ‘ t show a consistent relationship to endotoxemia in our study , as did EF .

Lew et al. [17] , in their study on mice , have shown that recurrent exposure to subclinical endotoxin induces cardiac fibrosis and increased mortality . LPS increased left ventricle expression of collagen Ia1 , collagen IIIa1 , and other fibrosis markers . They have also shown that LPS increased mortality , and arrhythmias occurring few hours before death .

On comparing mean age of cardiac hemodialysis patients using high flux (Group A) and low flux dialyzer (Group B) , we didn ‘ t find any significant difference between them .(P = 0.187) .This could mean that high flux dialyzer didn ‘ t provide a longer survival span for cardiac patients , than low flux dialyzer .This could be due to the presence of highest percentage of accumulated endotoxemia within these two groups , with the highest percentage existing within cardiac high flux group A .

Mean age of non – cardiac low flux HD patients (Group D) was surprisingly higher than that of non – cardiac high flux HD patients (Group C) , (P = 0.051) . This was confirmed by a significant Odds Ratio (Sig = 0.006 , OR = 0.211 , 95 % CI = 0.069 – 0.645) .This was not only due to the less hemodynamic compromise of cardiac functions (the first cause of death in HD patients) , occurring in low flux dialyzers , providing a longer survival for those patients , but also to the obviously lower percentage of patients with accumulated endotoxemia within group D .

On comparing mean age in cardiac high flux (Group A) (having the highest percentage of patients with accumulated endotoxemia) and non – cardiac high flux (Group C) (having an obviously lower percentage of patients with accumulated endotoxemia) , it was significantly higher in cardiac group , (P = 0.002) .This was confirmed by a significant Odds Ratio (Sig = 0.004 , OR = 1.067 , 95 % CI = 1.021 – 1.114) . This means that neither hemodynamic cardiac burden of high flux dialysis nor accumulated endotoxin , had deleterious impact on those patients survival . Also , on comparing cardiac low flux (Group B) (having a higher percentage of patients with accumulated endotoxin) and non – cardiac low flux (Group D) , age was significantly higher in the cardiac group , (P = 0.016) .This was confirmed by a significant Odds Ratio (Sig = 0.027 , OR = 1.068 , 95 % CI = 1.007 – 1.131) .This could mean that , in our study , neither the type of dialyzer nor the accumulated endotoxin has affected much the survival span of cardiac patients , or possibly because older patients usually have more co – morbid condition than younger ones & may be also longer dialysis duration with all its long term complications .

In our study , we didn ‘ t find significant difference as regards gender distribution on comparing cardiac high flux (group A) and cardiac low flux (group B) , (both having predominant male gender , P = 0.118) , and also both having the highest percentage of patients with accumulated endotoxin) . This same situation existed on comparing cardiac low flux (group B) (having more than 65 % of its patients with accumulated endotoxemia) and non – cardiac low flux (group D) (having the least percentage of patients with accumulated endotoxemia) , as both also having higher male percentage ,(P = 0.190) .

On the contrary , we found significant difference in gender distribution between non – cardiac high flux (group C) , (having higher female percentage and more than 65 % of its patients with accumulated endotoxemia) and non – cardiac low flux (group D) , ((having higher male percentage and the least percentage of patients with accumulated endotoxemia) , (P = 0.004).This was confirmed by a significant Odds Ratio (Sig = 0.006 , OR = 0.211 , 95 % CI = 0.069 – 0.645 . This could mean that up to a certain extent males are not much more prone to develop accumulated endotoxemia than females and this topic has to be subjected to further study on a much larger scale . Significant difference in gender distribution existed between cardiac high flux (group A) ,(having higher male percentage and also having the highest percentage of patients with accumulated endotoxemia) and non – cardiac high flux (group C) ,(having higher female percentage and also more than 65 % of its patients with accumulated endotoxemia) .This was confirmed by a significant Odds Ratio (

Sig. =0.002 , OR = 5.714 , 95 % CI = 1.021 - 1.114) .

Dry weight wasn' t much affected by high and low flux dialyzers , except on comparing cardiac high flux (Group A) patients and non - cardiac high flux (Group C) patients , (P = 0.020) , reflecting cardiac dysfunction effect , may be the male gender predominance and also the much higher percentage of patients with accumulated endotoxin within the cardiac group , leading to an obvious increase in dry weight of this group .This was confirmed by significant Odds Ratio (Sig = 0.026 , OR = 1.027 , 95 % CI = 1.003 – 1.052) . Dry weight didn ' t differ significantly between cardiac and non – cardiac low flux dialyzed patients .

Mcintyre et al.[3] , reported that UF volume was the only factor having influence on endotoxemia level with an r^2 of 0.43 , and P < 0.001 .

BMI , duration of HD , UF rate , serum albumin , and predialysis systolic and diasyolic blood pressure didn ' t affect our results , as they didn 't show any significant difference on comparing each of the studied groups to the other groups .

Pump speed was higher in cardiac high flux (group A) than each of cardiac low flux (group B) , (P = 0.000) , and non – cardiac high flux (group C) , (P = 0.037) , and it was also higher in cardiac low flux (group B) than non – cardiac low flux (group D) , (P = 0.001) , reflecting the hemodynamic burden which could be linked to the cardiac function status of these patients being overtly cardiac and may be also linked to increased gut microbacteria translocation by increased hemodynamic stress , considering that cardiac high & low flux group A & B had the highest percentages of patients with accumulated endotoxin .

Urea reduction ratio % was highest in cardiac high flux group A (with highest percentage of patients with accumulated endotoxemia , and having the most affected cardiac EF) ,and in non – cardiac high flux group C (having more than 65 % of its patients with accumulated endotoxemia) ,and this means that the efficient high URR % overcomes the problem of increased endotoxemia in high flux dialysis groups . Cardiac high flux group A had a significantly higher URR % than cardiac low flux group B (p = 0.001) (confirmed by a highly significant Odds Ratio (Sig = 0.003 , OR = 1.055 , 95 % CI = 1.018 – 1.094) , and a non – significantly higher URR % than non – cardiac high flux group C (P = 0.587) .This implied that URR % didn 't have a direct relationship to accumulated endotoxemia & EF .URR% was significantly higher in non- cardiac low flux group D (having the least percentage of patients with accumulated endotoxin , and a better EF) , as compared to cardiac low flux group B (P = 0.054) and non – significant difference existed between non – cardiac low flux group D and non – cardiac high flux group C .

Two controlled trials compared on – line hemodiafiltration within either low – flux [18] , or high – flux HD [19] . In both studies , no differences could be observed at primary analysis .

Oshvandi et al.[20] , in their study that compared high flux and low flux dialysis as regards their effect on predialysis blood urea nitrogen , which was found to be higher in high flux than low flux dialysis , in a statistically non – significant way .

. ***Akanda et al.***[1], reported that a significant association has been found between blood urea nitrogen level and the presence of coronary artery disease.

HsCRP was significantly higher in non – cardiac low flux group D as compared to non – cardiac high flux group C (P = 0.029) , and this was against the expectation as group D had the least percentage of patients with accumulated endotoxin levels . This was confirmed by a significant Odds Ratio (Sig = 0.048 , OR = 0.977 , 95 % CI = 0.955 – 1.000) . HsCRP didn ' t show any other significant results within our study and didn ' t affect our results , so we couldn ' t accurately link HsCRP level increase to accumulated endotoxemia percentage within our patients .

Hiroyuki et al.[21], in their study reported that there was a significant positive relationship between low – grade LPS and CRP suggested contributing to systemic inflammation in hemodialysis patients .

Chu et al.[22], reported that the high – flux dialyzer with synthetic polysulphone membranes failed to provide a better anti – inflammatory or antioxidative effect than the low - flux dialyzer .

Claire et al.[23], documented higher anti – inflammatory effect of high flux than low flux dialysis , and reported statistically significant difference in the rate of change of inflammatory markers , (including C – reactive protein) between high and low flux dialysis patients , after adjustments for baseline variables .

Mcintyre et al.[3], showed a positive correlation between HsCRP and predialysis endotoxin . This situation didn ' t exist in our study .

CONCLUSION

Cardiac high flux and low flux HD patients showed a higher percentage of patients with accumulated endotoxin levels than non – cardiac high flux and low flux HD patients . Endotoxemia was higher in cardiac high flux than low flux patients , and in non – cardiac high flux than low flux patients .

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Table (1) : Comparison of Group A & Group B as Regards Endotoxoxemic Parameters and Cardiac Disease Measurements :

		Group A	Group B	t	P – value
Predialysis Mean±SD		0.26± 0.06	0.26 ± 0.08	-0.167	0.868 ‡
Endotoxin	**Range**	0.1 – 0.38	0.11 – 0.45		
Postdialysis Mean ±SD		0.25 ± 0.08	0.28± 0.13	-1.094	0.278‡
Endotoxin	**Range**	0.1 - 0.45	0.11 – 0.63		
Endotoxin	**Zero**	16 (55.2 %)	11 (35.5 %)		
DELTA change Decrease Increase		13 (41.9 %) 7 (22.6 %)	5 (17.2 %) 8 (27.6 %)	4.486	0.106†
EF	**Mean ±SD**	49.06 ±13.60	55.76±13.14	1.941	0.057‡**
	Range	25 – 72	30 – 70		
EF	**> 75 %**	0(0.0 %)	0 (0.0 %)		
Category	**55 – 75 %**	12 (38.7 %)	19 (65.5 %)		
	40 – 54 %	11 (35 . 5%)	9 (31.0 %)	7.222	0.065†
	30 – 39 %	7 (22.6 %)	1 (3.4 %)		
	< 30 %	1 (3.2 %)	0(0.0 %)		
LVH	**-VE**	19 (61.3 %)	15 (51.7 %)	0.558	0.455†
	+VE	12 (38.7 %)	14 (48.3 %)		
Effusion	**-VE**	29 (93.5 %)	26 (89.7 %)	0.297	0.586†
	+VE	2 (6.5 %)	3 (10.3 %)		
AF	**-VE**	31 (100 %)	29 (100.0 %)	NA	NA †
	+VE	0 (0.0 %)	0(0.0 %)		

**** Significant ‡ Independent t – test †Chi – square test NA = not applicable**

TABLE (2) : Comparison Of Group C & Group D As Regards Endotoxemic Parameters And Cardiac Disease Measurements :

		Group C	Group D	t	P –value
Predialysis	**Mean ±SD**	0.26 ± 0.12	0.26 ± 0.10	-2.012	0.949‡
Endotoxin	**Range**	0.1 -0.5	0.09 – 0.5		
Postdialysis	**Mean ± SD**	0.33 ± 0.12	0.30 ± 0.11	-1.037	0.304‡
Endotoxin	**Range**	0.1 – 0.5	0.1 – 0.52		
Endotoxin	**Zero**	11 (39.3 %)	10 (31.2 %)		
DELTA change	**Decrease**	8 (28.6 %)	8 (25.0 %)	0.872	0.647†
	Increase	9 (32.1 %)	14 (43.8 %)		
EF	**Mean ± SD**	63.56 ± 7.95	62.07 ± 5.48	0.834	0.408‡
	Range	48 – 84	52 – 70		
EF	**> 75 %**	2 (6.2 %)	0 (0.0 %)		
Category	**55 – 75 %**	27 (84.4 %)	27 (96.4 %)		0.253†
	40 - 54 %	3 (9.4 %)	1 (3.6 %)	2.746	
	30 – 39 %	0 (0.0 %)	0 (0.0 %)		
	< 30 %	0 (0.0 %)	0 (0.0 %)		
LVH	**- VE**	21 (65.6 %)	11 (39 . 3 %)	4.163	0.041†**
	+VE	11 (34.4 %)	17 (60.7 %)		
Effusion	**-VE**	29 (90.6 %)	28 (100.0 %)	2.763	0.096†
	+VE	3 (9.4 %)	0 (0.0 %)		
AF	**-VE**	31 (96.9 %)	28 (100.0 %)	0.89	0.346†
	+VE	1 (3.1 $)	0 (0.0 %)		

** Significant ‡ Independent t – test † Chi – square test

TABLE (3) : Comparison of Group A & Group C as Regards Endotoxemic Parameters and Cardiac Disease Measurements

		Group A	Group C	t	P – value
Predialysis	**Mean ± SD**	0.26 ± 0.06	0.26 ± 0.12	0.102	0.919 ‡
Endotoxin	Range	0.1 – 0.38	0.1 – 0.5		
Postdialysis	Mean ± SD	0.25 ± 0.08	0.33 ± 0.12	-1.747	0.086‡
Endotoxin	Range	0.1 – 0.45	0.1 – 0.5		
Endotoxin	Zero	11 (35.5 %)	11(39.3 %)		
DELTA	Decrease	13 (41.9 %)	8 (28.6 %)	3.556	0.169 †
change	Increase	7 (22.6 %)	9 (32.1 %)		
EF	Mean ±SD	49.06 ± 13.60	63.56± 7.95	-5.184	0.000‡***
	Range	(25 – 72)	(48 – 84)		
EF	> 75 %	0(0.0 %)	2 (6.2 %)		
Category	55 – 75 %	12 (38.7 %)	27 (84.4 %)		
	40 – 54 %	11 (35.5 %)	3 (9.4 %)	20.330	0.000†***
	30 – 39 %	7 (22.6 %)	0 (0.0 %)		
	< 30 %	1 (3.2 %)	0 (0.0 %)		
LVH	-VE	19 (61.3 %)	21 (65.5 %)	0.128	0.721†
	+VE	12 (38.7 %)	11 (34.4 %)		
Effusion	-VE	29 (93.5 %)	29 (90.6 %)	0.184	0.668†
	+VE	2 (6.5 %)	3 (9.4 %)		
AF	-VE	31 (100 %)	31 (96.9 %)	0.984	0.321†
	+VE	0 (0.0 %)	1 (3.1 %)		

*** Highly Significant ‡Independent t – test †Chi – square test

Table (4) : Comparison of Group B & Group D as Regards Endotoxemic Parameters and Cardiac Disease Measurements

		Group B	Group D	t	P –value
Predialysis	Mean ±SD	0.26 ± 0.08	0.26 ± 0.10	-1.945	0.057 ‡ **
Endotoxin	Range	0.11 – 0.45	0.09– 0.5		
Postdialysis	Mean ± SD	0.28 ± 0.13	0.30 ± 0.11	-1.290	0.203‡
Endotoxin	Range	0.11 – 0.63	0.1 – 0.52		
Endotoxin	Zero	16 (55.2 %)	10 (31.2 %)		
DELTA change	Increase	8 (27.6 %)	14 (43.8 %)		
EF	Mean ± SD	55.76 ± 13.14	62.07 ± 5.48	-2.698	0.009 ‡ ***
	Range	30 – 70	52 – 70		
EF	> 75 %	0 (0.0 %)	0 (0.0 %)		
Category	55 - 75 %	19 (65.5 %)	27 (96.4 %)		
	40 – 54 %	9 (31.0 %)	1 (3.6 %)	8.776	0.012†
	30 – 39 %	1 (3.4 %)	0 (0.0 %)		
	< 30 %	0 (0.0 %)	0 (0.0 %)		
LVH	-VE	15 (51.7 %)	11 (39.3 %)	0.888	0.346†
	+VE	14 (48.3 %)	17 (60.7 %)		
Effusion	-VE	26 (89.7 %)	28 (100.0 %)	3.057	0.080 †
	+VE	3 (10.3 %)	0 (0.0 %)		
AF	-VE	29 (100.0 %)	28 (100.0 %)	NA	NA
	+VE	0 (0.0 %)	0 (0.0)		

**Significant ***Highly Significant ‡Independent t- test †Chi – square test NA = not applicable