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ASSOCIATION OF ENDOTOXIN IN PRE AND POST HEMODIALYSIS

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Abstract

Background: Endotoxemia is widely reported phenomenon in hemodialysis (HD) patients. Lipopolysaccharide (LPS) is a major structural component of the outer membrane of Gram-negative bacterial cell wall. Patients undergoing hemodialysis 'three times per week' can be exposed to 300–600 litre of water depending on their prescription. All kinds of treatment processes applied in this study have improved dialysis water purity and reduced levels of endotoxin.

Methodology: This study includes total 58 samples of pre & post dialysis 29 CKD patients with age and sex matched undergoing dialysis treatment in Hemodialysis unit of a tertiary care hospital Melmaruvathur Tamil Nadu. Endotoxin measurement was done by Human serum endotoxin, ET GENLISATM ELISA 96 test kit. All Statistical analysis in the study performed using SPSS for window version 20.0. The results summarized as mean ± Standard deviation (SD) and a two-tailed P-value less than 0.05 was considered to be statistically significant.

Result: The concentration of endotoxin level in pre-dialysis (1.3300 ± .80291) is increased and decreased in post- dialysis (1.2103 ±.66365) The endotoxin level between 29 samples of pre-dialysis and 29 samples of post- dialysis showed no significant difference 0.519 ($p<0.05$).

Conclusion: Endotoxiemia in hemodialysis patients is reduced by the use of dialyzer and dialyzing fluid. The dialyzer membrane made of Sevelamer lowers endotoxin levels. To improve patient outcome, the ultimate goal of Hemodialysis center is to achieve high quality, safe hemodialysis water treatment and dialysate by use of ultrapure fluids. The centers should emphasize and educate the importance and training to their employees as well as supporting adequately resourced infection control programs.

KEYWORDS: Endotoxin, CKD, dialyzer membrane and water dialysate.

INTRODUCTION

Endotoxemia is widely reported phenomenon in hemodialysis (HD) patients. (1,2) End Stage Renal Disease (ESRD) patients have increased morbidity and mortality compared to the general population. Infection is the second most important cause of the increased mortality seen in these ESRD patients (3). End-stage renal disease (ESRD) is associated with persistent elevated plasma concentrations of pro-inflammatory cytokines. Patients with ESRD have a higher risk to acquire infections than the general population, and septicemia is one of the most severe types of infection. (4)

Chronic kidney disease (CKD) is an important and independent risk factor for cardiovascular disease (CVD) and death (5). In an ongoing search for determinants underlying the increased incidence of adverse outcomes

in CKD, subclinical endotoxemia may be an attractive factor to explore. The human gut is host to 100 trillion commensal organisms, which contributes to an enteric reservoir of about 1 g of endotoxin (6). Impaired gut barrier function in CKD could permit translocation of gut-derived endotoxin into the systemic circulation. (7-9)

The Endotoxins (lipopolysaccharide in the outer wall of gram negative bacteria) can generate a complex host response through signaling pathways initiated after attachment of lipopolysaccharide (LPS) to the CD14 antigen on effector cells (10). The progressive accumulation of uremic toxins is supposed to contribute to loss of the intestinal epithelial barrier integrity, gut bacterial translocation (GBT), dysbiosis, and chronic inflammation (11, 12). Endotoxins are complex, amphiphilic macromolecules of up to 1000 KD in molecular weight, making free glomerular filtration unlikely, supported by research showing endotoxin is not present in sterile urine (13)

LPS is a major structural component of the outer membrane of Gram-negative bacterial cell wall. It is composed of three structural domains: an amphipathic lipid A, a core oligosaccharide and an Oantigen polysaccharide (14,). The lipidA, structure is conserved at the species level and plays a major role in bacterial pathogenicity (15) and immunogenicity (16). LPS is considered as a main pathogen-associated molecular pattern (PAMP) (17)

There are three potential sources of LPS exposure in patients with CKD: (a) bacterial translocation across the gastrointestinal barrier; (b) use of bactericidal systemic antibiotics, leading to the release of LPS during bacteriolysis; (18, 19) and (c) the potential use of non-ultrapure water for preparation of the dialysate in the hemodialysis population. (20,21)

Bacterial LPS is a constituent of the outer membrane of Gram-negative bacteria. It is a potent stimulator of the host inflammatory response, and it has a key role in the pathogenesis of bacterial sepsis, a major cause of mortality in critically ill and hospitalized patients. Although both the polysaccharide and lipid portions of the LPS molecule contribute to the pathogenic potential of Gram-negative bacteria, many of the toxic effects elicited by LPS are mediated by lipid A, its biologically active moiety. (22) Lipid A activates host cells including macrophages, neutrophils, and endothelial cells, resulting in the generation and release of inflammatory mediators. (23)

Exposure to bacterial structures, such as lipopolysaccharides (LPS) yields an inflammatory response mediated by innate immunity (24). This inflammatory response to LPS in ESRD has been demonstrated to be potentialized by uremic toxins and contributes to altered immune response dysfunctions observed in chronic kidney disease (CKD) (25).

Elevated systemic markers of inflammation are commonly observed among patients with kidney failure on maintenance dialysis. (26, 27) These inflammatory markers have been closely linked to cardiovascular events and protein-calorie malnutrition, two strong predictors of morbidity and mortality in this patient population. (28) LPS has been detected in the peripheral circulation of patients in states of extracellular fluid volume expansion, including those with heart failure and CKD. (29,30)

More than 75% of deaths in these patients are as a result of septicemia (31). The incidence rate of bacterial infections in ESRD patients is one episode per 100 patient months (32, 33). These bacterial infections are often life threatening given the increased susceptibility of uremic patients to infection due to their immune dysfunction (34). While Staphylococcus aureus is the major pathogenic organism (33) responsible for infections in dialysis patients, it has been found that endotoxemia due to gram-negative organisms is also a potential source of inflammation in these ESRD patients. (35)

Of the patients treated by dialysis, over 383,900 receive maintenance hemodialysis. Patients undergoing hemodialysis 'three times per week' can be exposed to 300–600 l of water depending on their prescription (36, 37). The volume of dialysis fluid increases for those on nocturnal treatments to 580–860 l per week (37).Endotoxin fragments or endotoxin in the dialysate bath may pass through the dialyzer membranes or cause transmembrane stimulation of circulating immune cells to produce symptoms of septicemia or a pyrogenic reaction. The presence of dialysate contaminants also triggers inflammatory markers, such as high

sensitivity C-reactive protein, interleukin (IL)-6, fibrinogen, and intercellular adhesion molecule (sICAM-1) (38)

Inflammation during hemodialysis may occur in some manners. Bio-incompatibility between dialyzer and blood, the endotoxin in dialysis fluid, access-related infections, and the glucose degradation products have been contributed to the inflammation responses during hemodialysis (39). It has been surmised that endotoxin in dialysis fluids gains access to the patient's bloodstream via the dialyzing membrane. The permeability of hemodialysis membranes to endotoxin was tested directly in only one study which reported transfer in two of six trials with coil and Kiilhemodialyzers (40).

Pyrogenic reactions have been reported as a frequent complication in hemodialysis patients (41) the pyrogenicity of endotoxin (42) and the frequent colonization of hemodialysis water systems by gram-negative bacteria (43) suggest that endotoxin is involved in hemodialysis-associated pyrogenic reactions. In the literature, three lines of indirect evidence have implicated endotoxin as the pyrogen responsible for these reactions: (a) detection of antibody in hemodialysis patients to endotoxins extracted from bacteria present in dialysate (44,45) (b) Limulus lysate reactivity of plasma from hemodialysis patients experiencing pyrexia (46-48), and (c) association of pyrogenic reactions with gram-negative bacterial contamination of hemodialysis fluids (48, 49).

Ensuring the necessary quality of dialysate is a vital aspect of this type of treatment considering the repeated, large volumes each patient is subjected to. Specifically, chemical, bacterial, and associated endotoxin contamination can threaten a dialysis patient’s health. Dialysis patients often have additional comorbidities (e.g., diabetes, hypertension, cardiovascular disease, etc.) that can make them more vulnerable to adverse outcomes. Aging, obesity, and hypertension rates are also increasing in the U.S. population, which are associated with ESRD and chronic kidney disease (50)

Endotoxins (bacterial lipopolysaccharide) are proposed to be a major contributory factor to the chronic inflammatory state seen in patients with end-stage kidney disease (ESKD), and particularly in those on dialysis therapy. (51, 52) Chronic inflammation is associated with poor prognosis in dialysis patients (53) and endotoxin-lowering strategies could potentially be useful in improving clinical outcomes in this population. However, blood endotoxin detection is difficult and no endotoxin detection assay has been validated for use in patients with ESKD. The optimum method of endotoxin detection needs to be determined in patients with ESKD to facilitate the development of endotoxin-lowering strategies in the future. Endotoxins can be detected using the Limulus amoebocyte lysate (LAL) assay. (54)

It is important to determine the optimum detection assay for use in patients with end-stage kidney disease (ESKD) since endotoxemia is reported to be associated with chronic inflammation (55) – itself a poor prognostic marker (53). Accurate endotoxin measurements are essential to further understanding of the sequela of endotoxemia in this population and to facilitate the development of potential endotoxin lowering strategies (56)

Therefore, this present study is to determine the level of endotoxin and association between pre and post hemodialysis patients.

Materials and Method:

Study design: This study was carried out at Melmaruvathur Adhiparasakthi Institute of Medical science and research, Tamil Nadu, India and approved by institutional ethical committee number: ECR/1487/Inst/TN/2020 MAPIMS/IEC/52/2022, based on ICMR guidelines on biomedical research in human beings and clinical practice. The written informed consent was obtained from participants voluntarily involved in the study.

Study subject: This study includes total 58 samples of pre & post dialysis 29CKD patients with age and sex matched undergoing dialysis treatment in Hemodialysis unit of a tertiary care hospital Melmaruvathur Tamil Nadu. Inclusion criteria of the study are CKD of both genders over 18 to 75 years old, who were undergoing dialysis treatment for more than six months and were dialyzed two to three times weekly each time for 3-5 hours with polysulfone dialyzing membranes. Patients with active infection, malignancy, bone marrow disease or haemoglobinopathy, clinical evidence of blood loss were excluded from the study.

All patients had been on regular hemodialysis for at least 2 months and were dialyzed twice weekly each time for 3-5 h with cellulose (n = 20) or polyacrylomtrile (n = 2) dialyzing membranes.

The data collected from the following basic demographic information such as age (years), sex, dialytic vintage (months), cardiovascular comorbidities, diabetes mellitus, body weight (BW; kg), and body mass index (BMI; kg/m2).

Blood samplingandanalysis: All blood samples were taken before and after a dialysis session with rapid separation of serum and storage at -85˚C before endotoxin measurement.

Methodology: Endotoxin measurement was done by Human serum endotoxin, ET GENLISA™ ELISA 96 test kit- QU/22-23/2711. The method employs sandwich ELISA technique. Human endotoxin, ET monoclonal antibodies are pre-coated onto micro wells. Samples and standards are pipetted into microwells and Human endotoxins (ET) present in the sample are bound by the antibodies. Biotin labeled ET antibody is added and followed by Streptavidin- Horse radish peroxidase (HRP) is pipetted and incubated to form a complex. After washing microwells in order to remove any non-specific binding, the substrate solution TMB (3, 3`, 5, 5`Tetramethybenzidine) is added to microwells and colour develops proportionally to the amount of Human endotoxin, ET in the sample. Colour development is then stopped by addition of stop solution. Absorbance is measured at 450 nm.

Standard, Human ET (Concentrated, 320 EU/L) is 0.5 ml. Standard Calibration Range is 10 EU/L to 160 EU/L. The Serum samples Coagulated at room temperature for 10-20 minutes and centrifuged for 20-min at 2000-3000 rpm. 50 microliter of prepared Standards added to respective standard wells. 40 microliter Samples are added to respective sample wells. 10 microliter of Biotinylated ET Antibody pipetted to respective sample wells.50 microliter of Streptavidin: HRP Conjugate pipetted to all wells and then mixed well. Plate covered with a sealer and incubated for 60 minutes at 37°C. Aspirated and washed the plate for 4 times with diluted Wash Buffer (1X) and blot residual buffer by firmly tapping plate upside down on absorbent paper. Liquid wiped from the bottom outside of the microtiter wells as any residue can interfere in the reading step.100 microliter of TMB Substrate pipetted to all wells. Plate incubated at 37°C for 10 minutes.100 microliter of Stop Solution pipetted to all wells. The wells turned from blue to yellow in color and the absorbance read at 450 nm with a microplate within 10-15 minutes after addition of Stop solution.

Statistical analysis: All Statistical analysis in the study performed using SPSS for window version 20.0. The results of laboratory tests in the study to be summarized as a mean ± Standard deviation (SD) (Descriptive statistics), Chi-square test (Categorical variables) and Independent‘t’ test (comparing with two groups) and correlation between parameters by Pearson correlation analysis. A two-tailed P-value less than 0.05 was considered to be statistically significant.

Table: Comparison of endotoxin between Pre-dialysis and post-dialysis

Paired Samples Statistics					
Absorbance		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Pretest	1.3300	29	.80291	.14910
	Posttest	1.2103	29	.66365	.12324

Paired Samples Test									
Absorbance		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Pretest - Posttest	.11966	.98654	.18320	-.25560	.49491	.653	28	.519

RESULT

This cross-sectional study consist of 58 samples; 29 as pre-dialysis and 29 as post-dialysis, compared endotoxin levels between 29 samples of pre-dialysis and 29 samples of post-dialysis by using students paired t- test. The concentration of endotoxin level in pre-dialysis(1.3300 ± .80291) is increased and decreased in post- dialysis (1.2103 ±.66365) The endotoxin level between 29 samples of pre-dialysis and 29 samples of post- dialysis showed no significant difference 0.519 ($p<0.05$).

DISCUSSION

CKD patients have higher prevalence of inflammation (57) which is an independent risk factor for cardiovascular events through promotion of atherosclerosis (58). Infection being the 2nd most common cause of death in hemodialysis patients (59), bacterial infections especially by gram negative bacteria serves as a major contributor (60). Endotoxin (Lipid A), a glucosamine based phospholipid, is the hydrophobic anchor of lipopolysaccharide and makes up the outer monolayer of the outer membranes of most gram-negative bacteria (14).

Endotoxins enter the blood circulation from bacterial translocation as well as from the use of a re-processing dialyzer. Terminal renal patients who undergo re-processing hemodialysis did not have endotoxemia both prior to and following hemodialysis unless they associated with infection, or other complications. (61)Exposure to endotoxin, a profoundly proinflammatory stimulus, results in release of a wide variety of proinflammatory cytokines and binding via CD14 to systemic immune competent cells (62). It results in a broad range of negative cardiovascular (CV) effects including peripheral vasodilation and reduction in cardiac contractile performance (63) Endotoxin (without sepsis) was initially proposed as a stimulus for immune activation in the proinflammatory state of congestive heart failure (64).

Hemodialysis using a re-processing dialyzer could increase the risk of infection. The risk of infection could occur due to entry of endotoxin from the dialyzer and dialyzing fluid. The potential for exposure of dialysis patients to greater levels of microbial and endotoxin contamination has increased dramatically with the increase in reuse of hemodialyzers, and the use of bicarbonate dialysate and high flux dialysis. There is a concern that endotoxins or bacteria may cross or interact at the membranes of these dialyzers, triggering the release of endogenous pyrogens (cytokines) by peripheral blood mononuclear cells to cause pyrogenic reactions (PR).Pyrogenic reactions are a well-recognized complication of hemodialysis and have been associated with dialyzer reuse, high-flux dialysis, and bicarbonate dialysate. However, the roles of bacteria and endotoxin in dialysate for producing PR are not well defined. If such condition continues, it may cause chronic inflammation, increasing the long-term morbidity and mortality of patients with terminal renal failure who undergo hemodialysis. (61)

Dialysis patients are characteristically volume overloaded. Hemodialysis (HD) in combination with ultrafiltration results in significant systemic hemodynamic perturbation and clinically significant reduction of regional perfusion in critical organs such as the heart (65-67). Such repeated ischemic injury to this vulnerable vascular bed results in acute cardiac injury, long-term myocardial damage, and increased mortality. (67, 68) It has been shown previously that patients on long-term maintenance HD have evidence of mucosal ischemia (69) and ultrafiltration causes a reduction in splanchnic blood volume (70) despite preserved blood pressure (BP) (71). Endotoxin contamination of dialysis water has long been recognized as a cause of CV instability during dialysis (72)

Endotoxin is released by bacterial cell wall breakdown within and beyond the gut lumen, from effective host defense mechanisms and by autolysis. Endotoxin enters the circulation via bacterial translocation (passage of intact bacteria and macromolecules such as endotoxin across the intestinal barrier (73), with bowel edema and hypoperfusion being the two main factors influencing bowel wall permeability in congestive heart failure (74). The permeability or impermeability of membranes to large molecules is dependent upon pressure gradient and the resultant membrane stretching, as well as the initial pore size and thickness. (75) Hemodialysis imposes a discrimination by molecular size in the rate of solute transfer such that smaller solutes having higher

membrane permeability are removed at a faster rate than are larger solutes. With ultrafiltration, membrane permeability to larger molecules increases and permits a transfer rate close to that of smaller molecules (76)

If endotoxin passes through a dialysis membrane, about 3.5 x l0 ng/min could be transferred during ultrafiltration of 500 ml of contaminated dialysate over a 3-hour period (12,500 ng/ml x 500 mlll8O mm). At a flow rate of 200 ml/min, a single pass through the hemodialyzer should result in an endotoxin concentration of about 175 ng/ml in the sterile circuit outlet line (3.5 X 10 ng/min 200 ml/ min). The LLA in our studies had a minimum sensitivity of 0.015 ng of endotoxin standard per milliliter. Therefore, the maximum endotoxin transfer by solvent drag must have been less than 0.000 1 of that for smaller molecules (0.015 ng/ml 175 ng/ml).(77) This low transmittance coefficient (<0.01%) is expected for a molecule as large as endotoxin (approximate molwt, 10^6daltons (42), since the reported coefficient for the smaller albumin molecule (molwt, 44,000 daltons) is 0.2% (76). In a report of endotoxemia in febrile reactions during hemodialysis, Raij, Shapiro, and Michael (78) measured dialysate endotoxin concentrations as low as 5 x 10 to 5 x 102 ng endotoxin/ml.

In clinical hemodialysis, the higher pressure in the blood compartment limits the potential for macromolecule transfer from dialysate to blood. In contrast to normal clinical conditions, the pressure gradient in most of our experiments was reversed to permit ultrafiltration of dialysate and to improve the potential for transfer of macromolecules to the sterile compartment. Even under these favorable conditions, the transfer of Limulus lysate-reactive material was not detected. Dialysate cultures in our experiments contained at least 10 bacterial ml and as much as 12,500 ng of endotoxin equivalents per milliliter, levels which are substantially higher than those reported to be associated with pyrogenic reactions. (77)

Antibody to endotoxin that has been detected in patients dialyzed with the Kiilhemodialyzer (44,45) may be explained by trace amounts of endotoxin passing through an intact dialyzing membrane. During long-term hemodialysis, however, occasional blood leaks or contamination of the dialyzer blood compartment may also account for exposure to endotoxin. (77) Furthermore, patients with chronic renal failure have been reported to be more susceptible to infection (79) and, therefore, the antibody detected in patients on hemodialysis may be in response to infection acquired by routes other than parenteral exposure during hemodialysis. Although specific antibody production indicates exposure to endotoxin, conclusions regarding membrane permeability to endotoxin cannot be substantiated (77)

We have demonstrated that significant endotoxemia is common in patients with advanced CKD. Endotoxemia appears to be aggravated by initiation of dialysis and is higher in those HD patients with the greatest degree of dialysis-induced hemodynamic instability, who also exhibit high degrees of dialysis-induced myocardial stunning. Elevated levels of circulating endotoxin are significantly associated with reduced survival (80). In our study also the endotoxin level was slightly higher in pre-dialysis than post-dialysis.

The levels seen in patients receiving dialysis are extremely high, comparable with those reported in severe liver disease (81) HD itself appears to be responsible for increasing exposure to translocated intestinal endotoxin, as evidenced by a large difference between patients with very severe CKD stage 5 but not yet started on dialysis and those receiving dialysis. Predialysis CKD stage 5 patients are very similar for demographic factors and comorbidities when compared to patients established on HD. After commencing HD, patients swiftly demonstrated a marked increase in endotoxemia, potentially resulting from dialysis-induced splanchnic hypoperfusion (80).

The Bruneck Study showed that elevated plasma levels of endotoxin are associated with CVD in the general population (82). Endotoxemia has also been shown to be related to inflammation and atherosclerosis in peritoneal dialysis patients (35) Nevertheless, identification of gut bacteria as the source of endotoxin, a likely source of endothelial injury, provides a convenient target for reducing the greatly increased cardiovascular risk in kidney transplant and all CKD patients.(83)

We did not observe an increase in circulating levels of endotoxin during HD therapies, although post-HD levels of endotoxin still significantly correlated with ultrafiltration volume. Translocation may occur predominantly in the postdialytic period, which we did not have access to samples from. Other possibilities

are that there was sequestration of endotoxin during the HD treatment as an effect of monocyte activation, which is commonly seen during extracorporeal circulation, or by direct adsorption onto the dialysis membrane. (80) The polysulfone material used in most of these treatments is well described as having a potent ability to adsorb endotoxin and a wide variety of other circulating substances (84), deriving its high biocompatibility status from the ability to buffer complement and other factors within the reactive cascade (80)

Once water enters a hemodialysis center, the goal is to achieve high quality and safe hemodialysis water and dialysate. Water treatment, system design, and distribution material choices are contributing factors. Dialysis water treatment should remove chemical and microbial contaminants to below established allowable limits and is characterized by two phases: (i) pretreatment, where constituents are removed from the feed water to protect the downstream treatment components and (ii) water treatment, which is the process of physically removing and/or chemically inactivating remaining chemical and/or microbial contaminants. Details regarding water treatment options and typical designs have already been given (85-87)

The changing water treatment at municipalities due to the nation's variable water quality, rapid developments in membrane technology and water disinfection, and strains on our health system are important discussion points for the future. However, the patient should be their own best advocate by being knowledgeable about the potential hazards that poor water quality can cause in hemodialysis. For improved patient outcomes, the ultimate goal is to eventually transition to the use of ultrapure fluids as the technology improves and to move toward a common evidence-based standard that is accepted internationally. Thus, more individuals will probably need renal replacement therapy (maintenance hemodialysis, peritoneal dialysis, or transplantation). Asserting that water and dialysate quality is an important factor in protecting the health of hemodialysis patients is an understatement (88)

All kinds of treatment processes applied in this study have improved dialysis water purity and reduced levels of endotoxin. Hybrid treatment using ultrafilter, ozone and hydrogen peroxide for disinfection was the most efficient treatment in reducing endotoxin concentration of dialysis water. (89)

We speculate that the lowering of systemic inflammation by sevelamer may be mediated by, among other mechanisms, LPS binding by sevelamer. In a recent in vitro study, we showed that sevelamer shows LPS-binding properties, resulting in the lowering of endotoxin levels in an aqueous solution (90) In a subsequent observational cross-sectional study conducted in 46 patients with chronic kidney failure on maintenance hemodialysis, we found that plasma endotoxin levels were significantly lower among patients prescribed sevelamer compared with those who were prescribed either calcium-based binders or no binders (91)

Reducing the level and/or activity of LPS may therefore be a novel yet important therapeutic strategy in CKD. In recent years, the potential role of LPS in inflammation has led to growing interest in interventions that may reduce and/or neutralize its activity, such as sevelamer. This has stimulated research efforts to decipher the apparent anti-inflammatory properties of this phosphate binder, as the mechanism(s) underlying this effect is not well understood. Emerging studies provide some indirect evidence that sevelamer may bind LPS and sequester bile acid–LPS complexes in the intestinal tract. It is postulated that this could limit the translocation of bacterial products from the intestinal lumen into the bloodstream. Although this might be an important mechanism by which sevelamer attenuates systemic inflammation, a clinical trial is required to test this hypothesis in a large population of patients with CKD. (92)

Strength of the study is the level of endotoxin in post hemodialysis patients reduced than pre hemodialysis. The limitations of the study are the sample size (N= 58) pre and post samples of 29 hemodialysis patients. Our study was endotoxin assay in human serum Elisa Kit, cross sectional study between pre and post hemodialysis but microbiological assay to be checked in water by LAL(Limulus lysate assay) and to find the correlation of endotoxin in water and serum of hemodialysis patients and comparative study to be done with healthy controls in association with soluble CD14, C-reactive protein, inflammatory markers interleukin (IL 6, IL8), complete blood count, lipid profile and biochemical parameters.

CONCLUSION

Endotoxiemia in hemodialysis patients is reduced by the use of dialyzer and dialyzing fluid. The dialyzer membrane made of Sevelamer lowers endotoxin levels. (90)To improve patient outcome, the ultimate goal of Hemodialysis center is to achieve high quality, safe hemodialysis water treatment and dialysate by use of ultrapure fluids. The centers should emphasize and educate the importance and training to their employees as well as supporting adequately resourced infection control programs. (88, 89)

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