

## Original Research Article

# Dyslipidemia and oxidative stress are causative factors for atherosclerosis changes in hemodialysis patients

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**Received:** 20 August 2019

**Accepted:** 26 August 2019

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## ABSTRACT

**Background:** Cardiovascular disease is one of the leading cause of death in chronic kidney disease. The increased cardiovascular mortality observed in all stages of Chronic kidney disease patients. In hemodialysis cardiovascular mortality is more than 60%. In hemodialysis dyslipidemia contribute for the triggering of atherosclerosis. Endothelial dysfunction and oxidative stress are serves as main precursor for the progression of atherosclerosis. So the present study was aimed at studying lipid profile and oxidative stress in hemodialysis patients.

**Methods:** A cross sectional study carried out over a 2 year period in Department Nephrology and General Medicine OPD, MIMS, Vizianagaram, Andhra Pradesh, India. A total of 60 hemodialysis patients are included. In all the participants Lipid profile, SOD, MDA and Serum Nitrate was measured.

**Results:** There is a significantly increased levels of serum triglycerides and VLDL in hemodialysis patients when compared with Control. The HDL-C was significant Lower in hemodialysis patients when compared with control. The serum total cholesterol and LDL-C not shown any significant change. The Serum MDA and Serum Nitrate was significantly higher in hemodialysis patients compared with Control and it is statistically significant ( $p < 0.001$ ). Whereas the serum SOD value was significantly decreased in hemodialysis patients when compared with control and it is statistically significant ( $p < 0.001$ ).

**Conclusion:** Present study finding suggested that the incidence of atherosclerosis changes are higher in hemodialysis patients. Early detection and correction of atherosclerosis changes can help us to reducing the deleterious effects.

**Keywords:** Cardiovascular disease, Hemodialysis, Lipid profile, Oxidative stress

## INTRODUCTION

Cardiovascular disease is one of the leading cause of death in chronic kidney disease. The increased cardiovascular mortality observed in all stages of Chronic kidney disease patients.<sup>1</sup> CKD stage 3 to stage 4 mortality occur due to cardiovascular causes rather than decline of renal function and the mortality rate is 15-30% times higher than the control group.<sup>2</sup> In hemodialysis patients cardiovascular mortality is more than 60%.<sup>3</sup> In hemodialysis patients dyslipidemia contribute for the

triggering of atherosclerosis. Oxidative stress and Endothelial dysfunction, are serves as main precursor for the development and progression of atherosclerosis.<sup>4</sup>

In hemodialysis patients both qualitatively and quantitatively abnormalities of plasma lipids. The most common abnormalities in hemodialysis patients is increased triglycerides due to decreased clearance of Very low density lipoprotein (VLDL). and decreased high-density lipoprotein (HDL).<sup>5</sup> In dialysis patient there is more of a dyslipidemia rather than hyperlipidemia.

This may be a risk factor for atherosclerosis complication leading to mortality and morbidity in chronic kidney disease patients.<sup>6</sup>

Reactive Oxygen Species (ROS) are continuously produced from the routine cellular physiology.<sup>7</sup> But derangement in the production lead to oxidative stress. hemodialysis is pro-oxidant state. The degree of oxidative stress depends on production of free radicals and concentration of antioxidants.<sup>8</sup> In hemodialysis patients due to oxidative stress causes lipid peroxidation and which can indirectly assay by malondialdehyde(MDA) and antioxidant status can be estimated by measuring superoxide dismutase (SOD).<sup>9</sup>

Increased oxidative stress will causes reducing availability of nitric oxide by converting into peroxynitrite. which will further cause endothelial dysfunction and subsequently shows effect on vascular function.<sup>10</sup> All the conditions causes changes in the vascular permeability and entrance of Low density lipoprotein (LDL) into the intima. Here it is oxidized due to oxidative stress and initiates inflammatory process.<sup>11</sup>

## METHODS

The present study is a cross sectional study carried out over a 2 year period that is from June 2017 to June 2019 in Department of Nephrology and General Medicine OPD, MIMS, Vizianagaram, Andhra Pradesh, India. Those who were hemodialysis patients and attending nephrology unit over a one year period were taken as subjects for the present study. A total of 60 patients from hemodialysis were included in this study. Patients attending nephrology unit other than hemodialysis, Patients with any debilitating illness and hemodialysis patients who did not provide inform constant were excluded. To all Participants the importance of the study and procedure to be performed were informed. Informed consent was obtained from all the participants. A questionnaire was given to all patients and detailed clinical examination was performed.

In all the participants blood pressure measured by using sphygmomanometer both systolic and diastolic blood pressure was measured based on 1<sup>st</sup> and 5<sup>th</sup> korotkoff phase. All the participants are subjected 12 lead Electrocardiography and recorded at paper speed 25mm/s and 1-mV/cm calibration.

In all these participants, blood urea was estimated by GLDH – Urease method.<sup>12</sup> Serum creatinine was estimated by Jaffes method.<sup>13</sup> Based on serum creatinine, estimated GFR (eGFR) was computed by the Modification of Diet in Renal Disease (MDRD).<sup>14</sup> The serum total cholesterol and HDL-C were analyzed using cholesterol oxidase method,<sup>15,16</sup> triglyceride assessment was estimated by glycerol kinase method,<sup>17</sup> LDL-C was calculated by using Friedwald formula.<sup>17,18</sup> serum SOD activity was estimated by Kakkar et al, method and serum

MDA level was estimated by Thiobarbituric acid method.<sup>19,20</sup> serum nitrate will be estimated by colorimetric Griess assay.<sup>21</sup>

All the data was expressed in Mean and Standard deviation (mean±SD). Statistical significance between control and cases groups Z test was performed using Microsoft Excel and SPSS software 16.0. The statistical significance was determined at 5% (p <0.05) level.

## RESULTS

The present study was conducted at Maharajah's Institute of medical sciences, vizianagaram, Andhra Pradesh, India. A total of 120 subjects were included in which 60 are hemodialysis patients and 60 are control.

Table 1 shows the mean age of the hemodialysis patients was 47.29 years ±10.09 Control it was 43.29 years ±10.78. As regards the sex distribution, the majority of subjects were male in hemodialysis 58% and Control 56%. The diagnostic criteria like blood urea and serum creatinine were significantly higher in hemodialysis patients when compared to Control. eGFR was significantly decreased in hemodialysis patients when compared with control. In the present study systolic and diastolic blood pressure was significantly increased in hemodialysis patients compared with Control (p<0.001).

**Table 1: Demographic features and diagnostic parameters in controls and hemodialysis patients.**

	Hemodialysis patients	Control
Number	60	60
Age (mean±SD) years	47.29±10.09	43.29±10.78
Sex (males %)	58	56
(females%)	42	44
Blood urea (mg/dl)	84.22±28.12	16.72±10.01**
Serum Creatinine (mg/dl)	7.28±3.28	0.76±0.24**
eGFR (mL/min)	14.57±7.69	98.57±8.73**
<b>Blood pressure (mm Hg)</b>		
Systolic	151.45±19.87	110.18±8.28**
Diastolic	94.21±8.73	75.20±4.23**
<b>Type of ECG changes</b>		
LVH	N=32	N=0
Ischemic changes	N=28	N=0

\*\*=p<0.001

Table 2 shows significantly increased levels of serum triglycerides and VLDL in hemodialysis patients when compared with Control. The HDL-C was significant Lower in hemodialysis patients when compared with control. The serum total cholesterol and LDL-C not shown any significant change.

**Table 2: Comparative study of serum lipid profile in control and hemodialysis patients.**

Parameters	Hemodialysis patients	Control
Serum Triglycerides (mg/dl)	185.22±17.23**	113.8 ±17.83
Serum Total cholesterol (mg/dl)	172.61±21.78	169.26±13.17
Serum HDL-C (mg/dl)	28.67±3.83**	43.52±4.26
Serum LDL-C (mg/dl)	106.90±22.96	102.98±13.65
Serum VLDL (mg/dl)	37.04±3.82**	22.76±3.56

**Table 3: Comparative study of serum MDA, serum nitrate and SOD in control and hemodialysis patients.**

Parameters	Hemodialysis	Control
MDA (nmol/ml)	7.21±0.64**	1.96±0.58
Serum Nitrate(μmol/L)	33.84±2.24	10.21±2.32
SOD (U/ml)	3.24±0.78**	8.12±2.21

Table 3 shows the Serum MDA and Serum Nitrate was significantly higher in hemodialysis patients compared with Control and it is statistically significant ( $p < 0.001$ ). Whereas the serum SOD value was significantly decreased in hemodialysis patients when compared with control and it is statistically significant ( $p < 0.001$ ).

## DISCUSSION

In the present study Blood urea and serum creatinine were increased in hemodialysis patients due decreased glomerular filtration. The blood pressure also significantly increased in hemodialysis patients due to hypervolemia and uncontrolled hypertension.

The most common abnormality in hemodialysis patients is hyperlipidemia. In the present study serum triglycerides was significantly increased due to high production and low catabolism of triglycerides. The causes are decreased lipoprotein lipase (LPL) activity due to presence of LPL inhibitors in hemodialysis patients.<sup>22</sup> In addition dialysis patients repeated use of heparin causes depletion of LPL. These factors causes decreased degradation of triglycerides rich lipoprotein like chylomicron and VLDL and causes hypertriglyceridemia.<sup>23</sup> In the present study serum cholesterol was not shown significant changes in control and hemodialysis patients. Previous studies observed hypercholesterolemia with heavy proteinuria and concluded that heavy proteinuria will causes changes in the HMG CoA reductase and hepatic LDL receptor.<sup>24</sup> In the present study proteinuria was minimal so no change in cholesterol value. Vasilis et al, also reported no

change in serum cholesterol value.<sup>25</sup> In the present study serum LDL was not shown significant difference between control and hemodialysis patients elevated LDL is common in nephrotic syndrome and not a feature of hemodialysis.<sup>26</sup> In the present study serum HDL was significantly decreased in hemodialysis patients compared to control. The main cause for decreased HDL is due to decreased apoprotein A-I and A-II, which are main constituents of HDL.<sup>27</sup> The decreased Lecithin cholesterol acyltransferase (LCAT) and increased Cholesteryl Ester Transfer Protein (CETP) also contribute decreased serum HDL. In the present study VLDL was significantly increased due to increased CETP and decreased LPL.<sup>28</sup>

In hemodialysis patients the serum MDA was significantly higher when compared with Control the main cause is continues production of free radicals.<sup>29</sup> This is may be due to bio incompatibility of dialysis membrane and entry of hydrophilic compounds to the dialysate and influx of toxin from dialysate. All the factors leads activation of macrophages and produce free radicals and which causes lipid peroxidation and produces MDA.<sup>30</sup> The serum SOD was significantly decreased in hemodialysis patients compared with Control the causes for decreased SOD are loss zinc and copper in dialysate fluid which act as cofactor for SOD and increased lipid peroxidation causes utilization of antioxidant enzymes. The decreased RBC life span also contribute decreased SOD level in hemodialysis patients.<sup>31</sup> All the above factors contribute increased free radicals which react with nitric oxide (NO) and produce peroxy nitrite which is an unstable molecule and it will be converted into nitrate. In the present study serum nitrate was significantly higher in hemodialysis patients when compared with control. The decreased nitric oxide causes vascular endothelial dysfunction and leads to atherosclerosis changes.<sup>32</sup>

From the findings of present study, it was concluded that there is a high prevalence of dyslipidemia in hemodialysis patients. Increased triglycerides decreased HDL contribute for formation of atherosclerosis. Increased MDA, serum Nitrate and decreased SOD contribute for the progression of atherosclerosis. Early detection and correction of atherosclerosis changes can help us to reducing the deleterious effects.

## ACKNOWLEDGEMENTS

The authors acknowledge the help and support provided by the Department of Nephrology, Maharajah's institute of medical sciences, Nellimarla, Vizianagaram district, Andhra Pradesh, India.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Varma BHVKP, Rao TM, Raju DSSK. Dyslipidemia and oxidative stress are causative factors for atherosclerosis changes in hemodialysis patients. *Int J Adv Med* 2019;6:1383-7.