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Endothelial Markers: Key Indicators and Therapeutic Targe Chronic Renocardiac Syndrome

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Abstract

Background: There is conflicting evidence regarding the relationship between endocan and cardiovascular disease (CVD in chronic kidney diseases. The present study aimed to assess endocan and proinflammatory marker levels in Renocardio syndrome.

Methodology: Out of 135 subjects, 85 were diagnosed with chronic kidney diseases, and 50 were normal healthy controls of either sex with an age group of 18-65 years. Out of 85, 45 had chronic kidney disease with cardiovascular complications, and 40 had chronic kidney disease without cardiovascular complications. Blood urea, Creatinine and hs-CRP levels were estimated by EM-200 fully automated machine. Endocan by ELISA Method.

Results: The SPSS 22.0 version was used to analyze the results. Compared to patients with chronic renal failure without cardiovascular complications and the control group, blood urea, hs-CRP levels, and endocrine levels were considerably higher in the former group. The relationship between hs-CRP and endocan is positively correlated (r=0.6998).

Conclusion: The study parameters' observed values emphasise how better prognosis for cardiovascular complications in individuals with chronic kidney disease correlates with risk prediction.

Keywords: Endothelial markers, chronic renocardiac syndrome, endocan, cardiovascular disease (CVD)

1. Introduction

Heart failure and renal impairment are common comorbid issues, with the kidney being the most closely linked to acute heart failure. Cardio-renal syndrome (CRS) occurs when the malfunction of heart or Kidney, that leads to defect in the other organs. Atherosclerosis, is one of the major possible causes of cardiorenal syndrome, that further results occurrence of myocardial infarction and stroke. Patients with CKD3-5D have a higher frequency of subclinical atherosclerotic lesions, with a larger increase in advanced stages after adjusting for sex, age, and diabetes [1, 2].

Individual with chronic kidney disease (CKD) have elevated levels of oxidative stress and chronic inflammation as a result of an imbalance between the body's increased production of reactive oxygen species and its weakened defenses against them. The endothelium may sustain cytotoxic damage as a result of this oxidative stress, which contributes to the etiology of vascular disorders. Abnormal vascular smooth muscle cell growth, elevated prothrombotic and proinflammatory potential, and reduced vasodilation capacity are the results of endothelial activation [3,4].

In response of endothelium activation, a soluble dermatan sulfate proteoglycan (Endocan), secreted and the same expressed by lung and kidney endothelial cells.It is an endothelial cell-specific molecule-1 (ESM-1)found in vascular endothelial cells that binds to integrin CD11a/CD18 on lymphocytes and monocytes, regulating immune responses, especially during inflammation. It's synthesis and secretion is up-regulated by growth factors and cytokines like VEGF-A, VEGF-C, IL-1, TNF, TGF-β1, and FGF-2. Endocan plays a significant role in modulating cellular invasion during inflammation. Blood levels of endocan can serve as a biomarker for inflammation severity and assess the efficacy of therapeutic interventions in inflammatory diseases [5, 6].

A decreased glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2 or damaged kidney structure is defined as chronic kidney disease (CKD). Its course is associated with a gradual loss of kidney function that can eventually leads to end-stage renal disease (ESRD), that further linked to increased mortality, particularly from cardiovascular diseases. A pathophysiology of cardiovascular disorder is linked to endothelial dysfunction, with chemical involved in inflammation. Endocan, a proven key factor in to display endothelial dysfunction, with prognostic value in CKD, among other conditions [7].It compromises vascular barrier integrity, leading to significant inflammatory responses in mice and human umbilical vein endothelial cells. Blood endocan levels can predict a patient's health and prognosis [8, 9].

Endothelial cell dysfunction, which includes a wide range of maladaptive changes in the endothelial cell functional phenotype linked with higher cardiovascular risk, is a major factor contributing to increased cardiovascular risk [10].To aid in the diagnosis and prognosis of cardiac illnesses, the current study is designed to assess Endocan and proinflammatory marker levels in Renocardio syndrome.

Materials and Methods

An observation and analytical design of study was conducted in the Department of Biochemistry, Pacific Medical College, Udaipur, Rajasthan.With the provision of extended facility, a total 135 subjects were enrolled from the Medicine department, Nootan Medical College and research centre, Visnagar, Gujarat in the duration two years (December2022-November2023). Out of 135 subjects, 85 were diagnosed with chronic kidney diseases, and 50 were normal healthy controls of either sex with an age group of 18-65 years. Out of 85, 45 had chronic kidney disease with cardiovascular complications, and 40 had chronic kidney disease without cardiovascular complications. Present study has been obtained ethical approval from institutional ethical committee from Nootan Medical College. Written and verbal consent were taken from all the subjects.

Sample Collection and Analysis

A serum sample was acquired by centrifuging 5 ml of the patient's intravenous blood at 5000 revolutions per minute for 8 to 10 minutes with aseptic procedures. Two ml of serum sample were kept for Endocan analysis by ELISA techniques. The automated EM-200 system was used to estimate the amounts of blood urea, creatinine, and hs-CRP amounts.

Glomerular filtration rate was calculated with the help MDRD equation by using a web calculator. The Modification of Diet in Renal Disease (MDRD) equation:

MDRD = 186 x (Serum Creatinine level -1.154) x (Age -0.203) x 1.212 (If black) x 0.742 (If female) in millilitres per minute per 1.73 m2.

Study tools: Data were collected in case record form (CRF). The CRF comprise of details regarding diagnosis, cause of renal failure, serum biochemical marker values etc.

Statistical Analysis: The data were entered into Microsoft office excel and analyzed by Statistical Package for Social Sciences (SPSS) version 21 for windowssoftware. Descriptive statistics were reported in the form of mean, standard deviation. Normal distribution of data was checked by Shapiro-Wilk test. Comparison between two groupsof serum biochemical markers was done by paired t-test. P-value < 0.05 was considered as statistically significant.

Result

The present study has correlated findings to the gender of the participants in the study. A total of 135 patients enrolled in the study, 85 (62.96%) were diagnosed for chronic renal failure and 50 (37.03%) were normal healthy controls. Out of Out of 85, 45(52.94%) had chronic kidney disease with cardiovascular complications, and 40 (47.03%) had chronic kidney disease without cardiovascular complications by the respective clinician and were retrospectively studied. Demographic data were also analyzed like on the basis of age and gender. In control group (n=50) the total number of female participants was 21 (42%) whereas, the number of male participants was 29 (58%). For CKD with CVD Group, the number of male and female participants was 27 (60%) and 18 (40%) respectively. For CKD without CVD Group, the number of male and female participants was 21 (52.5%), and 19 (47.5%), respectively.

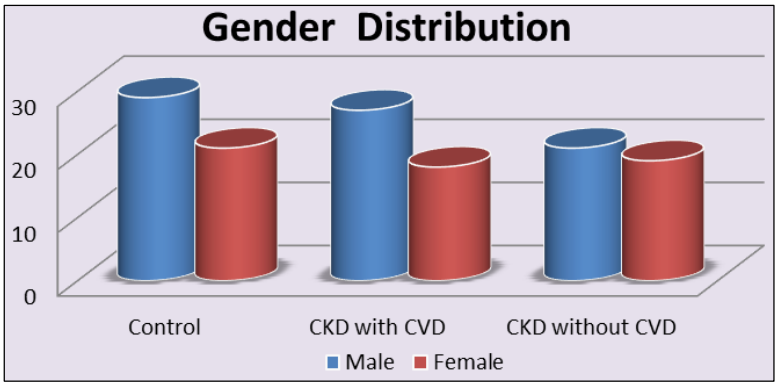
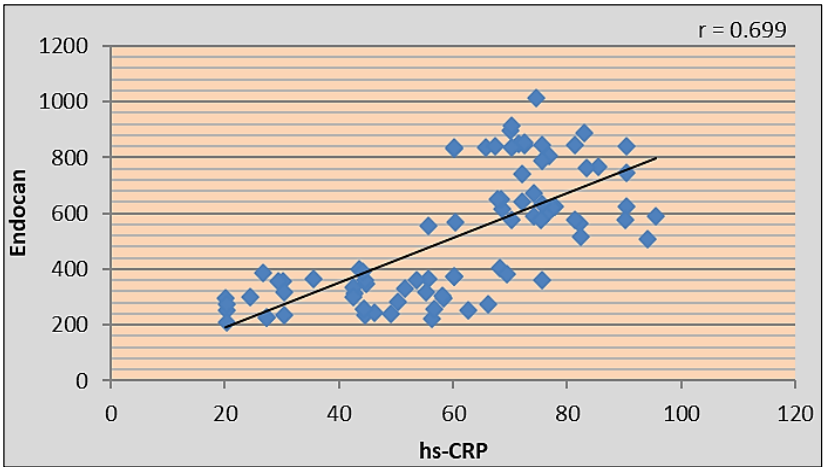


FIGURE1: GENDER DISTRIBUTION AMONG CARDIORENAL & CONTROL GROUPS

TABLE1: DESCRIPTIVE ANALYSIS OF STUDY VARIABLES

Study Groups	**Study Variables**					
	Age (Years) (Mean ±SD)	**eGFR (mL/min/1.73 m2) (Mean ± SD)**	**Creatinine (mg/dl) (Mean ± SD)**	**Urea (mg/dl) (Mean ± SD)**	**hs-CRP (mg/L) (Mean ± SD)**	**Endocan (Mean ± SD)**
Control	43.14±14.66	137.42±65.25	0.68±0.25	22.44±4.976	1.24±0.74	93.82±35.14
CKD with CVD	50.70±13.16	10.91±23.24	8.50±2.50	118.19±25.11	75.53±9.22	701.53±147.41
CKD Without CVD	43.33±14.22	7.18± 2.89	8.97±3.49	121.45±32.64	43.35±14.06	308.21±56.30
P Value	0.05*	0.001**	0.001**	0.001**	0.001**	0.001**

*: P value statistically significant & **: P value statistically highly significant.



GRAPH1: CORRELATION BETWEEN Hs-CRP &ENDOCAN AMONG CKD WITH CVD

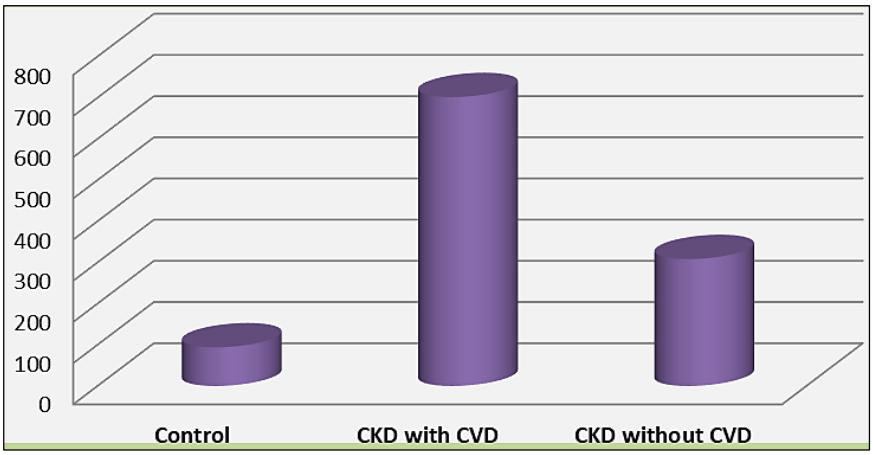


FIGURE2: ENDOCAN LEVEL IN OUR STUDY POPULATION

Discussion

A wide spectrum disorders involved both heart and kidney in which chronic dysfunction on one organ can lead acute or chronic dysfunction in another organ, which represents convergence of heart-kidney interactions across several interfaces. These include the hemodynamic cross-talk between the failing heart and the kidney responses and vice versa. This will lead to alternation in neurohormonal and inflammatory markers [11].Cardiovascular problems are the most common cause of mortality in people with renal failure receiving regular dialysis. Most people with progressive CKD die before renal failure.The accumulation of waste materials and toxins during kidney function exacerbates chronic inflammation, leading to CVD onset and progression. Recent theories suggest that vascular and peripheral blood cell senescence may contribute to CVDs in renal disease patients [12, 13].

A reduced baseline glomerular filtration rate (GFR) is usually associated with a worse prognosis for patients with heart failure (HF). This is because the kidneys filter blood, remove waste, and help regulate water and salt levels to control blood pressure. Reduced blood flow to the kidneys can injure them, which can lead to cardiorenal syndrome [14].In people with HF, every 10 ml/min decrease in estimated glomerular filtration rate (eGFR) increases the risk of all-cause death by 7%, while HF hospitalization in people with CKD increases the risk of all-cause death 3-7-fold [15].

Assessing the hs-CRP levels to the control, a substantial ($p<0.001$) rise is seen. Additionally, we found that patients with cardiovascular complications from CKD had a significantly higher level of hs-CRP ($p<0.001$) than patients with no cardiovascular complications of CKD (Table No.1). comparable findings reported by Adejumo OA *et al*.,[17] Davis Jones & Associates [18],&Idrissia Abdulmutallab& Associates [19],This implies that the inflammatory process in CKD patients does not start with dialysis and is not only tied to it because of the CKD patients. Various ideas have explained the relationship between inflammation and the decline in renal function.According to one view, renal failure and inflammation are linked via a decrease in nitric oxide synthase activity. Because nitric oxide synthase contributes to the synthesis of peroxynitrite, a crucial immune response mediator, it is associated with inflammation. The fact that end-stage renal disease results in decreased CRP filtration is one theory put out to explain greater CRP concentrations associated with CKD [20].Apart from its association with the

advancement of renal illness, CRP has demonstrated a robust predictive power for cardiovascular events in individuals with diminished renal function. Individuals in the group with cardiovascular complications. Elevated levels of fibrinogen have also been linked to acute coronary syndromes, including myocardial infarction and unstable angina. In comparison to the group of people without cardiovascular complications, the patients' fibrinogen concentration was considerably greater.Cytokines, particularly interleukin-6, which is produced by hepatocytes and activated macrophages, induce the secretion of fibrinogen and CRP [20].It has been proposed that interleukin-6 was the primary mediator involved in the synthesis of acute-phase inflammation proteins in acute myocardial infarction [19].

In comparison to the groups comprising healthy controls, those with illnesses groups had considerably greater endocan levels in the current investigation. Furthermore, compared to their counterparts with CKD without a cardiovascular disease problem, individuals with CKD with cardiovascular issue were shown to have considerably higher endocan levels (Table No.1). These results are consistent with previous studies. Serum endocan levels are considerably greater in CKD patients than in controls, according to research by Fatma M. El-Senosy*et al*.[20] Additionally, they observed a strong correlation between serum endocan levels and HD patients' much higher endocan levels relative to CKD patients.

When compared to CKD patients, HD patients showed a considerably larger carotid intima-media thickness (CIMT). Similar findings were made by Pawlak *et al*.[21] in their investigation.

A soluble glycoprotein i.e. plasma endocan levels are useful for the prediction for cardiovascular risk assessment in end stage renal diseases patients.The numerous literatures have mentioned its noteworthy associations between endocan levels and other indicators, such as soluble intercellular adhesion molecules (sICAM-1) and vascular cellular adhesion molecules (sVCAM-1), as well as tumour necrosis factor alpha (TNF-α), underscoring the role of endocan in vascular disease and inflammation. De Souza LV *et al*.,[22] observed that pediatric RT patients with both hypertension and a loss of renal function had noticeably higher endocan concentrations. By stimulating endothelial cells, releasing reactive oxygen species, and quickening the development of foam cells and atherosclerotic plaques, chronic inflammation accelerates the course of atherosclerosis at practically all phases.Currently, the prevailing consensus is that endocan primarily contributes to endothelial dysfunction in the development of atherosclerosis. When pro-inflammatory factors such as TNF-a, IL-1b, and others stimulate the expression of endocan, the levels of VCAM-1 and ICAM-1 rise as well. This improves the adhesion between leukocytes and endothelial cells and encourages the recruitment and migration of inflammatory cells [23].

Conclusions

- The present study highlighted increased plasma levels of endocan could be a promising predictor biomarkers cardiorenal complications among renal failure patients.
- The presented research shows that the endocan-mediated pathway can actively contribute to the inflammation, endothelial activation, so, it could be used as an inflammatory as well as endothelial dysfunction marker as well.
- More or less, Consequently, more study with large sample size require to precisely define endocan's function in the afore mentioned processes.

Endoocan is a novel inflammatory marker for atherosclerosis patients as well as a biomarker of endothelial dysfunction with significant therapeutic intervention potential. It is crucial for forecasting how CVD events will develop and how they will turn out. The presented research shows that the endocan-mediated pathway can actively contribute to the reciprocal relationships between uremia, inflammation, endothelial activation, and the prevalence of CVD via influencing soluble adhesion molecule. To enhance illness risk assessment and improve prognostic prediction, endocan can be detected. Cardiovascular events will become more common as a result of these disorders, while it is unclear how endocan contributes to these conditions. Consequently, more investigation is required to precisely define endocan's function in the aforementioned processes.

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