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Original Research

Association Of Serum Tumor Marker (Carcinoembryonic Antigen) With Chronic Kidney Disease In Indian Population

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ABSTRACT

Background: Chronic kidney disease (CKD) is one of the most important chronic, non-communicable diseases. CKD is a global health burden due to loss of renal function progressively and is a pathophysiological process with multiple etiologies which includes diabetes and hypertension. Carcinoembryonic antigen (CEA) is excreted by certain embryonic and adult tissues in addition to adenocarcinoma of the digestive organs, but its level is also high in chronic renal disorder. Our study was aimed to assess and compare the status of serum CEA level in chronic kidney disease subjects and healthy controls. **Materials and Methods:** Thecase-control study was conducted on 220 CKD patients.Cases (n = 220) were selected from the Medical OPD and ward of Jawahar Lal Nehru Medical College and Associated Group of Hospitals, Ajmer. Age and sex-matched healthy controls (n = 100) were selected from MOPD. The present study was approved by Institutional Ethical Committee. All samples were collected under aseptic conditions from the antecubital vein for estimation of biochemical parameters. **Results:** The mean activity of Serum CEA was significantly higher in CKD subjects as compared to healthy controls ($p < 0.0001$).Positive pearson correlation of serum creatinine with serum CEA was found ($r= 0.73$).**Conclusion:** Serum CEA can be used as a biomarker for the early detection of CKD in the general population to prevent the morbidity and mortality which are associated with CKD. If CKD is detected early and managed appropriately the deterioration in kidney functions can be slowed and the risk of cardiovascular diseases in renal patients can be reduced.

Keywords: Chronic kidney disease (CKD), Carcinoembryonic Antigen (CEA), End-stage renal disease (ESRD), Glomerular filtration rate (GFR), Chronic renal failure (CRF)

(**key words :** urinary tract infection(UTI), Escherichia coli, Antibiotic resistance)

INTRODUCTION

Chronic kidney disease (CKD) is one of the most important chronic, non-communicable diseases. CKD is a global health burden due to loss of renal function progressively and is a pathophysiological process with multiple etiologies. CKD is defined as kidney damage or glomerular filtration rate (GFR) <60 mL/min/1.73 m^2 for 3 months or more, irrespective of cause.[1]CKD represents an irreversible decline in GFR, in which there is a gradual loss of kidney function over a period of months to years. Causes of chronic kidney disease includes diabetes, high blood pressure, glomerulonephritis, and polycystic kidney disease.Loss of renal function is common in renal failure, irrespective of the underlying cause of the kidney disease.

Tumormarkers are bio-chemical substances that result as normal endogenous products that are produced at a greater rate in cancer cells or are the products of newly switched on genes that remained quiescent in the normal cells.[2]Tumor markers are used for clinical purposes such as screening, early detection, diagnostic confirmation, prognosis and prediction of therapeutic response, and monitoring disease and recurrence.[3]

Carcino-embryonic antigen (CEA) is a glycoprotein with a molecular weight of 180 KD, the protein content of which is approximately 40% and the carbohydrate approximately 60%.[4] It is excreted by certain embryonic and adult tissues in addition to adenocarcinoma of the digestive organs. Extensive studies of patients bearing primary and metastatic colorectal neoplasms have determined that

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its primary use is in the detection of local and metastatic cancer recurrence after initial resection of the primary tumor, through periodic post-operative analysis of CEA in serum or plasma.[5]Serial determination of the CEA is recommended with each course of treatment to help in predicting patient's response and monitoring the disease.[6] Direct injury, high metabolic demands or stimuli from renal dysfunction activate tubular cells, which produce cytokines, support inflammatory responses, causing further pathological changes in the renal parenchyma. It is generally accepted that the reticuloendothelial system is involved in CEA metabolism. CEA is initially taken up by Kupffer cells and then transferred to hepatocytes.[7,8] However, end-stage kidney disease induces altered regulation of pattern recognition receptors, leading to impaired macrophage function.[9] Further, persistent low-grade inflammation has been recognized as a common feature in patients with CKD.[10] Recent studies have also suggested that elevated serum CEA levels were associated with chronic low-grade inflammation status, such as carotid atherosclerosis and diabetes.[11-13] Therefore, changes in renal parenchyma metabolism and declining kidney function could reduce the renal clearance of CEA along with chronic inflammation leading to elevated serum CEA levels in CKD when compared to that of the control group. The serum CEA has prognostic importance in chronic renal disorder. Increasing levels signal a higher risk of ESRD mortality.

Serum urea and serum creatinine are widely accepted as the most common parameters to assess renal functions.The prevalence of CKD in general population was 16% in India.[14] If CKD is detected early and managed appropriately the deterioration in kidney functions can be slowed and the risk of cardiovascular diseases in renal patients can be reduced. This study was aimed to assess and compare the status of serum CEA in chronic kidney disease patients and healthy controls.

MATERIALS AND METHODOLOGY

The study was conducted on 220 chronic kidney disease patients. Patients were diagnosed as chronic kidney disease on the basis of clinical history, physical examination, serum urea and serum creatinine level. Cases were selected from the medical OPD and ward of Jawahar Lal Nehru Medical College and Associated Group of Hospital, Ajmer. Age and sex-matched healthy controls (n=100) were selected from Medicine OPD of Jawahar Lal Nehru Medical College and Associated Group of Hospital, Ajmer.

Inclusion criteria for the study group: Established cases of chronic kidney disease between age 30-60 years were taken.

Exclusion criteria

1. Acute kidney injury, acute infection, acute myocardial infarction, active liver disease or liver dysfunction, hematological and malignant overt diseases.
2. Cases associated with other inflammatory diseases such as cancer or autoimmunity.
3. Kidney transplant patients.
4. Pregnant and lactating women.
5. Lack of compliance with the protocol.
6. Patients who were unwilling to participate in the study were excluded.

Blood samples were collected after an overnight fast (12-14hrs) under aseptic conditions from all the study participants. All samples were centrifuged and analysed for serum urea, serum creatinine and serum CEA. Serum urea was measured by Urease-GLDH UV Enzymatic Kinetic method.[15] Serum creatinine was measured by Jaffe's Kinetic UV method.[16] Serum CEA was measured by Chemiluminescence Immunoassay method.[17]

Statistical Analysis

Data was represented in the form of table and graph and analysed statistically using SPSS and Microsoft Excel Spreadsheet. Mean ±SD was compared using equal or unequal variance unpaired student t-test and P value < 0.05 was considered significant. Pearson correlation was also performed.

RESULTS

The Table-1, Figure-1 shows the mean±SD level of serum urea (179.01 ± 33.39 v/s 23.36 ± 6.75) mg/dl, serum creatinine (7.37 ± 2.54 v/s 0.86 ± 0.52) mg/dl and serum CEA (6.60 ± 2.58 v/s 1.69 ± 0.45) ng/mL in chronic kidney disease subjects compared to healthy controls. The differences were statistically highly significant(P<0.0001).The Table-2, Figure-2 shows the serum CEA level in chronic kidney disease subjects. Figure-3 shows positive pearson correlation (r = 0.73) of serum creatinine with serum CEA in CKD patients.

Biochemical Parameters	Healthy Controls Subjects (n = 100) (Mean ± SD)	CKD subjects (n= 220) (Mean ± SD)	P VALUE
1. Serum urea (mg/dL)	23.36 ± 6.75	179.01 ± 33.39	P<0.0001*
2. Serumcreatinine (mg/dL)	0.86 ± 0.52	7.37 ± 2.54	P<0.0001*
3. Serum CEA (ng/mL)	1.69±0.45	6.60± 2.58	P<0.0001*

Table 1: Biochemical Parameters of Healthy Control Subjects v/s Chronic Kidney Disease Subjects

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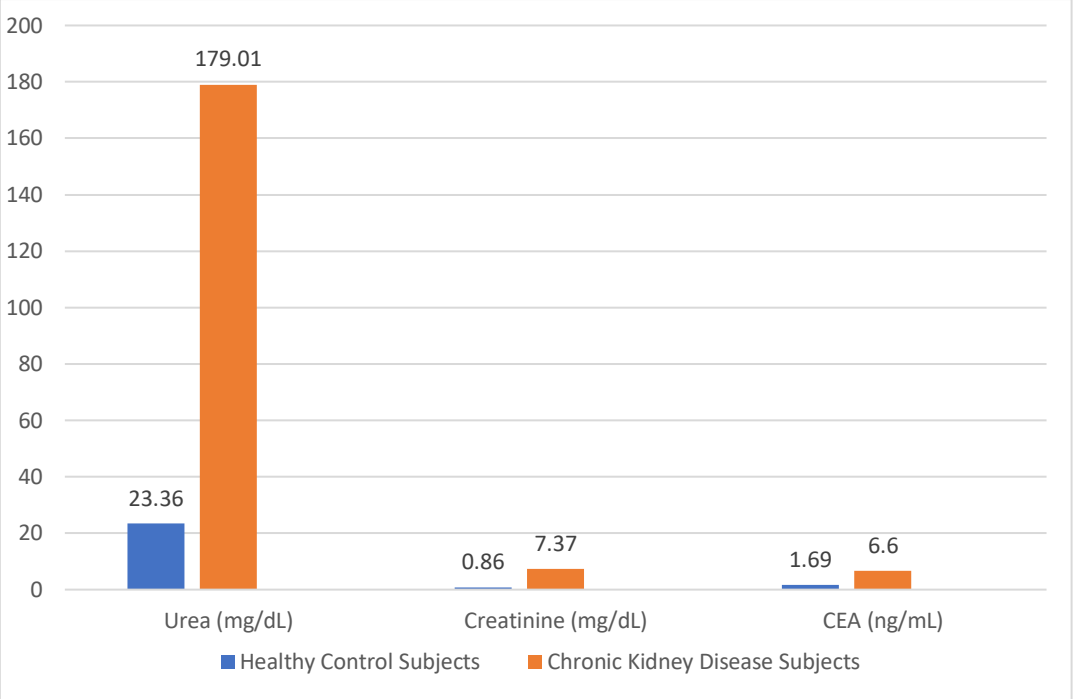

Figure 1: Comparison of Biochemical Parameters of Healthy Control Subjects V/S Chronic Kidney Disease Subjects

Table 2: Serum CEA levels in Chronic Kidney Disease Subjects

Serum CEA Level (ng/mL)	% Of Chronic Kidney Disease Subjects
< 3.0	11 %
3.1 – 6.0	33 %
6.1 – 9.0	37 %
9.1 – 12.0	18 %
> 12.0	1 %

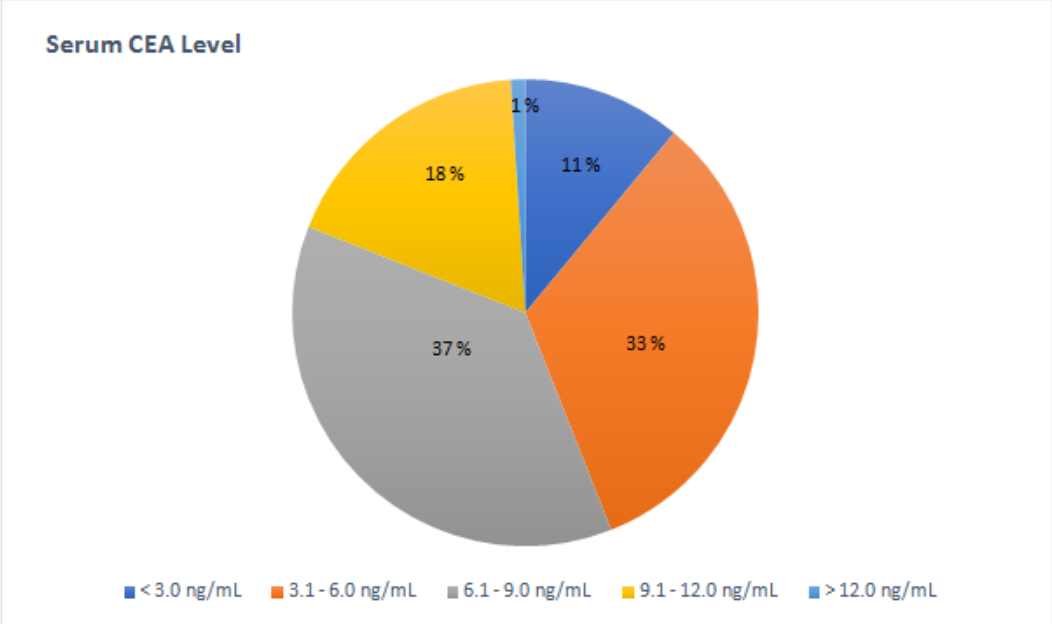

Figure 2: Serum CEA levels in Chronic Kidney Disease Subjects

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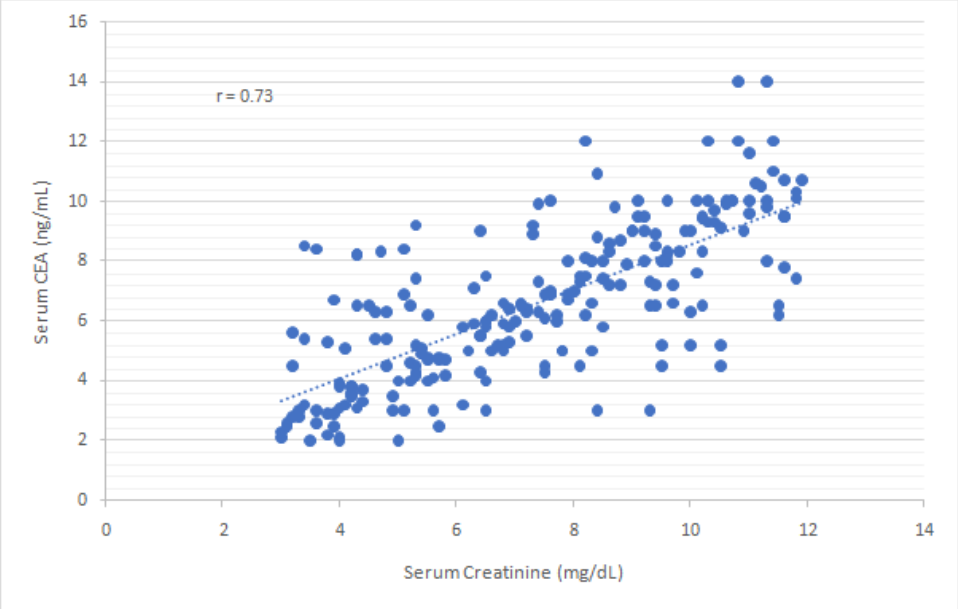

Figure 3: Pearson correlation of serum creatinine with serum CEA in CKD cases.

DISCUSSION

Chronic kidney disease is one of the most important chronic, non-communicable diseases. CKD is a global health burden due to loss of renal function progressively and is a pathophysiological process with multiple etiologies which includes diabetes, high blood pressure, glomerulonephritis and polycystic kidney disease. Other health conditions that may lead to CKD are obesity, high cholesterol, a family history ofkidney disease, lupus and other forms of cardiovascular diseases.

In the present study it was observed that the level of serum CEA was elevated in chronic kidney disease patients as compared to the healthy subjects (controls). Our findings are in agreement with Engin et al[18],Tzitzikos et al[19], Tong HL et al[20] and Rani BS et al[21] which also found that the mean activity of serum CEA was significantly higher in chronic kidney disease patients compared to the healthy subjects.

Increase in serum CEA is majorly due to injury to the renal parenchyma which is caused due to the activation of tubular cells which produces cytokines and starts inflammatory responses. Hence declining kidney function and changes in renal parenchyma metabolism due to pathological changes in the renal parenchyma , leads to elevated serum CEA levels in CKD patients. The observations of this study also revealed that 196 out of 220 chronic kidney disease patients have higher serum CEA levels(>3 ng/mL). Positive pearson correlation of serum creatinine with serum CEA was found (r= 0.73).

CONCLUSION

Serum CEA can be used as a biomarker for the early detection of chronic kidney disease in the general population to prevent the morbidity and mortality which are associated with chronic kidney disease.If CKD is detected early and managed appropriately the deterioration in kidney functions can be slowed and the risk of cardiovascular diseases in renal patients can be reduced.

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