CORRELATION OF CAROTID INTIMAL-MEDIAL THICKNESS WITH ESTIMATED GLOMERULAR FILTRATION RATE AND CARDIOVASCULAR RISK FACTORS IN PATIENTS OF CHRONIC KIDNEY DISEASE

Tejinder Sikri1, Ramesh Chander2, Pashaura Singh3, Sunil Kumar4, Kashmir Singh5, Saurabh Agarwal6, Pankaj Kumar7, Jagbir Singh8

1Professor, Department of Medicine, Government Medical College, Amritsar.
2Associate Professor, Department of Radio-Diagnosis, Government Medical College, Amritsar.
3Assistant Professor, Department of Medicine, Government Medical College, Amritsar.
4Junior Resident, Department of Medicine, Government Medical College, Amritsar.
5Senior Resident, Department of Medicine, Government Medical College, Amritsar.
6Junior Resident, Department of Medicine, Government Medical College, Amritsar.
7Junior Resident, Department of Medicine, Government Medical College, Amritsar.
8Junior Resident, Department of Medicine, Government Medical College, Amritsar.

ABSTRACT

BACKGROUND
Chronic Kidney Disease (CKD) is associated with premature mortality, decreased quality of life and increased health care expenditures. Many patients with CKD have cardiovascular disease and die prematurely from this condition instead of surviving long enough to face dialysis or transplantation. Carotid Intimal-Medial Thickness (CIMT) predicts future vascular events in the general population. However, the correlation of traditional cardiovascular risk factors and estimated glomerular filtration rate in Chronic Kidney Disease (CKD) with CIMT is not studied extensively. To determine the correlation of CIMT with traditional cardiovascular risk factors like age, Body Mass Index (BMI), dyslipidaemia and estimated glomerular filtration of CKD patients, CIMT was measured by means of high-resolution B-mode ultrasonography.

MATERIALS AND METHODS
In this randomised open study, in which 70 patients with chronic kidney disease at the Medicine/Nephrology Inpatients/Outpatients Department of the Guru Nanak Dev Hospital, Amritsar and 30 age and sex matched controls were enrolled. Data needed for the study was extracted from the files of patients. Estimated glomerular filtration rate was calculated by using Cockcroft-Gault (CG) formula. CIMT was measured using B-mode ultrasound.

RESULTS
- In our study, we found that CIMT in selected patients correlated significantly with traditional cardiovascular risk factors like age (r = 0.377, p-value = 0.00), systolic blood pressure (r = 0.517, p-value = 0.00), diastolic blood pressure (r = 0.487, p-value = 0.00), BMI (r = 0.223, p-value = 0.026), total cholesterol (r = 0.482, p-value = 0.00), LDL cholesterol (r = 0.210, p-value = 0.036), serum triglycerides (r = 0.636, p-value = 0.00), HDL cholesterol (r = 0.480, p-value = 0.00).
- Mean CIMT of smokers, diabetic was significantly higher as compared to non-smokers, non-diabetic patients and statistically significant (t-value = 2.53, p-value = 0.01), (t-value = 0.592, p-value = 0.557) respectively.
- Mean CIMT of CKD patients was (0.87±0.09) and healthy volunteers was (0.63±0.08). We further observed that CIMT in selected patients showed significant negative correlation with estimated glomerular filtration rate (r = -0.761, p-value = 0.00).

CONCLUSION
Therefore, it can be concluded that CIMT measurement by B-mode ultrasonography seems to be of clinical value in screening of CKD patients as an early marker of advanced atherosclerosis. Increased CIMT as an indicator of subclinical cardiovascular disease may help to identify such patients, who would benefit from aggressive therapeutic measures.

KEYWORDS
CIMT, CKD, Atherosclerosis, eGFR, Cardiovascular Disease.

with an increased risk of recurrent cardiovascular disease outcomes after adjustment for traditional cardiovascular disease risk factors.\textsuperscript{6,7} Some authors demonstrated that increased Carotid Intima-Medial Thickness (CIMT), which is clinically considered as the surrogate endpoint of cardiovascular disease which occurs early in the course of chronic kidney disease.\textsuperscript{8,9} These changes are associated with higher cardiovascular disease risk factors in patients with chronic kidney disease.\textsuperscript{10,11} Limited information is available on whether or not the decline in renal function is an independent risk factor for cardiovascular disease. The present study was undertaken to evaluate the same.

**MATERIALS AND METHODS**

In this randomised open study, in which 70 patients with chronic kidney disease at the Medicine/Nephrology Inpatients/Outpatients Department of the Guru Nanak Dev Hospital, Amritsar, and 30 age and sex matched controls were enrolled. Patients of acute renal failure, history of carotid surgery, age less than 18 years, those who were on hemodialysis or peritoneal dialysis, and patients having a previous history of ischaemic heart disease. Detailed history was taken and thorough general and systemic examination was done. Physical examination included height and weight measurements for calculating Body Surface Area (BSA). Routine baseline investigations were performed, i.e. Hb, TLC, DLC, PBF, ESR, Blood Urea and Serum Creatinine and Lipid Profile. Estimated Glomerular Filtration Rate (eGFR) was calculated by using Cockcroft-Gault (CG) formula using creatinine clearance (CrCl).

Carotid Doppler ultrasonography was performed by a single operator and the CIMT was measured using B-mode ultrasonound and a 7.5 MHz transducer. Intimal-medial thickness was defined as the distance between the leading edge of the first echogenic line (lumen-intima interface) and the second echogenic line (media-adventitia interface) of the far wall over the area devoid of atherosclerotic plaque.\textsuperscript{12,13} Three measurements were taken at 0.5, 1 and 2 cm below the carotid bifurcation of the common carotid artery on each side and their arithmetic averages were calculated. The intimal-medial thickness of both sides (right and left) was also calculated and the average of these two values was calculated. In this study, an atherosclerotic plaque is defined as a local thickness of intima greater than 1 mm or two times more than its adjacent normal layer.

**Statistical Analysis**

The statistical software SPSS Ver. 21 was used for statistical analysis. The mean ± standard deviation was calculated. Pairwise comparison between the cases and controls was performed for all parameters using student’s unpaired t-test. The values of P < 0.05 were considered as significant. Bivariate correlation analysis was used to see the correlation of different variables with CIMT.

**RESULTS**

A total of 70 CKD patients (32 males and 38 females) were enrolled in the study in Group A and 30 healthy volunteers (18 males and 12 females) were enrolled in the study in Group B. Mean age of Group A and Group B were 53.25 ± 16.47 and 38.86 ± 18.26, respectively. In our study, we found that CIMT in selected patients correlated significantly with traditional cardiovascular risk factors like age (r = 0.377, p-value = 0.00), systolic blood pressure (r = 0.517, p-value = 0.00), diastolic blood pressure (r = 0.487, p-value = 0.00), BMI (r = 0.223, p-value = 0.026), total cholesterol (r = 0.482, p-value = 0.00), LDL cholesterol (r = 0.210, p-value = 0.036), serum triglycerides (r = 0.636, p-value = 0.00), HDL cholesterol (r = -0.480, p-value = 0.00).

In our study, it was observed that there was statistically significant difference of CIMT between diabetic and non-diabetic patient (t-value = -0.592, p-value = 0.557). Mean CIMT of smokers was significantly higher as compared to non-smokers and statistically significant (t-value = 2.53, p-value = 0.01). Mean eGFR of Group A was (16.9 ± 7.8) and Group B was (112.22 ± 29.2) and there was statistically significant difference of eGFR distribution between the two groups (t-value = 25.3, p-value = 0.00). Mean CIMT of Group A was (0.87 ± 0.09) and Group B was (0.63 ± 0.08) and there was statistically significant difference of CIMT distribution between the two groups (t-value = -11.3, p-value = 0.00).

In our study, we further observed that CIMT in selected patients showed significant negative correlation with estimated glomerular filtration rate (r = -0.761, p-value = 0.00).

### Table 1. Comparison of Means of CKD Patients (Group A) and Healthy Volunteers (Group B)

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Variable</th>
<th>Mean of Group A (N = 70)</th>
<th>Mean of Group B (N = 30)</th>
<th>t-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Age (Years)</td>
<td>53.25 ± 16.47</td>
<td>49.13 ± 14.3</td>
<td>1.19</td>
<td>0.237</td>
</tr>
<tr>
<td>2</td>
<td>BMI (kg/m²)</td>
<td>28.1 ± 4.25</td>
<td>24.17 ± 2.96</td>
<td>-4.58</td>
<td>0.00</td>
</tr>
<tr>
<td>3</td>
<td>Systolic BP (mmHg)</td>
<td>154.3 ± 10.5</td>
<td>110.1 ± 7.5</td>
<td>-10.3</td>
<td>0.00</td>
</tr>
<tr>
<td>4</td>
<td>Diastolic BP (mmHg)</td>
<td>102.7 ± 14.8</td>
<td>79.0 ± 6.8</td>
<td>-8.35</td>
<td>0.00</td>
</tr>
<tr>
<td>5</td>
<td>Serum TC (mg/dL)</td>
<td>243.2 ± 37.7</td>
<td>187.4 ± 11.6</td>
<td>-7.92</td>
<td>0.00</td>
</tr>
<tr>
<td>6</td>
<td>LDL (mg/dL)</td>
<td>133.2 ± 29.9</td>
<td>115.0 ± 8.3</td>
<td>-3.21</td>
<td>0.002</td>
</tr>
<tr>
<td>7</td>
<td>HDL (mg/dL)</td>
<td>41.3 ± 4.0</td>
<td>49.1 ± 5.4</td>
<td>7.907</td>
<td>0.00</td>
</tr>
<tr>
<td>8</td>
<td>Serum Triglycerides (mg/dL)</td>
<td>343.7 ± 98.0</td>
<td>114.5 ± 18.1</td>
<td>-12.6</td>
<td>0.00</td>
</tr>
<tr>
<td>9</td>
<td>eGFR</td>
<td>16.9 ± 7.8</td>
<td>112.2 ± 29.2</td>
<td>25.3</td>
<td>0.00</td>
</tr>
<tr>
<td>10</td>
<td>CIMT (mm)</td>
<td>0.87 ± 0.09</td>
<td>0.63 ± 0.08</td>
<td>-11.3</td>
<td>0.00</td>
</tr>
</tbody>
</table>

the course of chronic kidney disease. These changes are associated with higher cardiovascular disease risk factors in patients with chronic kidney disease. Limited information is available on whether or not the decline in renal function is an independent risk factor for cardiovascular disease. The present study was undertaken to evaluate the same.

In our study, we found that CIMT in selected patients correlated significantly with traditional cardiovascular risk factors like age (r = 0.277, p-value = 0.00), systolic blood pressure (r = 0.257, p-value = 0.00), diastolic blood pressure (r = 0.387, p-value = 0.00). Study by Takato et al showed similar results for risk factors age and diabetes. Yilmaz et al in their study observed that IMT was independently associated with CKD stage and mean arterial pressure. Ekart et al found a statistically significant correlation between carotid IMT and the average one-monthly diastolic BP (p < 0.05) and ambulatory BP monitoring (p < 0.05).

In our study, we found that CIMT in selected patients correlated significantly with BMI (r = 0.223, p-value = 0.026), total cholesterol (r = 0.482, p-value = 0.00), LDL cholesterol (r = 0.210, p-value = 0.036), HDL cholesterol (r = -0.480, p-value = 0.00), serum triglycerides (r = 0.636, p-value = 0.00). Similar results were observed by Sется et al.

In our study, it was observed that there was statistically significant difference of CIMT between diabetic and non-diabetic patient (t-value = -0.592, p-value = 0.557). Study by Takato et al showed similar results for risk factors age and diabetes. Above mentioned findings were consistent with observations of Kawamoto et al. Similar observations were made by Sется et al. carotid IMT was significantly higher in patients with diabetes than in those without diabetes (0.930 ± 0.254 versus 0.794 ± 0.184; P = 0.002).

Mean of CIMT of smokers was significantly higher as compared to non-smokers and statistically significant (t-value = 2.53, p-value = 0.01). Similar results were shown by multiple regression analysis by Kawamoto et al. smoking status was significantly associated with CIMT.

Mean CIMT of Group A was (0.87 ± 0.09) and Group B was (0.63 ± 0.08) and that there was statistically significant difference of CIMT distribution between the two groups (t-value = -1.13, p-value = 0.00).

In our study, we further observed that CIMT in selected patients showed significant negative correlation with estimated glomerular filtration rate (r = -0.761, p-value = 0.00).

In another study, similar observations were made. Stepwise multiple linear regression analysis using IMT as an objective variable, adjusted by various factors as explanatory variables showed that eGFR was a significant independent contributing factor along with known risk factors in men (beta, -0.096; p = 0.018) and women (beta, -0.080; p = 0.035). Similar results were also found in another study. The reasons for the high CVD risk in patients with CKD remain unknown. A possible explanation is that decreased renal function may be associated with other non-traditional risk factors that were not evaluated in this study. Such factors include uric acid, homocysteine, C-reactive protein, albuminuria, oxidative stress, endothelial dysfunction and cytokines.

Chronic kidney disease may be complicated by both duration and severity of other causes of CVD and exacerbate atherosclerosis caused by CVD risk factors. The duration of

**DISCUSSION**

Some authors demonstrated that increased Carotid Intima-Medial Thickness (CIMT), which is clinically considered as the surrogate endpoint of cardiovascular disease, occurs early in

---

**Table 2. Comparison of Different Variables with CIMT**

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Correlation of Variables with CIMT</th>
<th>Correlation Coefficient (r value)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Age with CIMT</td>
<td>0.377</td>
<td>0.00</td>
</tr>
<tr>
<td>2</td>
<td>BMI with CIMT</td>
<td>0.223</td>
<td>0.026</td>
</tr>
<tr>
<td>3</td>
<td>SBP with CIMT</td>
<td>0.517</td>
<td>0.00</td>
</tr>
<tr>
<td>4</td>
<td>DBP with CIMT</td>
<td>0.487</td>
<td>0.00</td>
</tr>
<tr>
<td>5</td>
<td>TC with CIMT</td>
<td>0.482</td>
<td>0.00</td>
</tr>
<tr>
<td>6</td>
<td>LDL with CIMT</td>
<td>0.210</td>
<td>0.036</td>
</tr>
<tr>
<td>7</td>
<td>HDL with CIMT</td>
<td>-0.480</td>
<td>0.00</td>
</tr>
<tr>
<td>8</td>
<td>TG with CIMT</td>
<td>0.636</td>
<td>0.00</td>
</tr>
<tr>
<td>9</td>
<td>eGFR with CIMT</td>
<td>-0.761</td>
<td>0.00</td>
</tr>
</tbody>
</table>

---

**Figure 1. Comparison of CIMT of CKD Patients and Healthy Controls**

**Figure 2. Comparison of CIMT between Diabetic and Non-Diabetic CKD Patients**

**Figure 3. Comparison of CIMT between Smoker and Non-Smoker CKD Patients**

---

exposure to adverse CVD risk factors may be the largest in patients with pronounced CKD.

**SUMMARY AND CONCLUSION**

In this present study in which 70 patients with chronic kidney disease and 30 age and sex matched controls were enrolled.

In each patient, a detailed history, physical examination, laboratory evaluation and CIMT were recorded as per the proforma.

The Observations of this Study are Summarised as follows -

- Mean of Age, BMI, systolic blood pressure, diastolic blood pressure, total cholesterol, LDL cholesterol, VLDL cholesterol, serum triglycerides was significantly higher in CKD patients (Group A) as compared to healthy volunteers (Group B).
- Mean of HDL cholesterol was statistically significant lower in CKD patients as compared to control group.
- Mean of eGFR was also statistically significant lower in CKD patients as compared to control group.
- Mean CIMT was also statistically significant, higher in CKD patients as compared to control group.
- Mean CIMT was also statistically significant, higher in diabetic patients as compared to non-diabetics.
- Mean CIMT was also statistically significant, higher in smokers as compared to non-smokers.
- CIMT in selected patients showed statistically significant positive correlation with traditional cardiovascular risk factors like age, BMI, systolic blood pressure, diastolic blood pressure, total cholesterol, LDL cholesterol, VLDL cholesterol and serum triglycerides.
- CIMT in selected patients showed statistically significant negative correlation with HDL cholesterol and eGFR.

Therefore, it can be concluded that CIMT measurement by B-mode ultrasonography seems to be of clinical value in screening of CKD patients as an early marker of advanced atherosclerosis. Increased CIMT as an indicator of subclinical cardiovascular disease may help to identify such patients, who would benefit from aggressive therapeutic measures.

**Acknowledgement**

At the outset, I endow my sincere thanks to my supervisor, my mentor and my guide, Dr. Tejinder Sikri, MD, Professor, Department of Medicine, Government Medical College. This work could not have been possible without his immense efforts and guidance. I am grateful to him for his astute guidance that helped me to become a good clinician and above all a good human being.

At this stage, I would like to express my sincere gratitude to my Co-Supervisor, Dr. Ramesh Chander, MD, Associate Professor, Department of Radiodiagnosis, Government Medical College, Amritsar for his continuous support towards the study and research. I am indebted to Sir for his patience, support and enthusiasm for the Research work.

I am thankful to my Seniors, Colleagues and Juniors of Department of Medicine, Government Medical College, Amritsar without whose willing and wholehearted cooperation and optimistic and loving attitude it would have been impossible to complete this work the way it has been.

To my parents, Mr. Ranvirsingh and Mrs. Usha Rani and my younger brother Bhumiit and my sister Sangeet, I owe a special reverence for their unending and unconditional support, encouragement and blessings at every step of my life. It is a pleasure to thank my friends for their love and encouragement.

My words are not sufficient to express my gratitude to all my patients who peep behind every typed word of this project and without whose cooperation this project would not have seen the light of the day.

**REFERENCES**


