Screening of Asymptomatic Coronary Artery Disease in Type 2 Diabetes patients by TMT and its correlation with High Sensitivity C-Reactive Protein

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I. Introduction
Coronary artery disease is a relatively common and asymptomatic disease in Type 2 Diabetic patients. Hence the diagnosis of coronary artery disease is difficult in initial phase of disease. This gained special attention over recent years, since it has significant morbidity and mortality and coronary artery disease is one among the most common cause of death in Diabetic individuals with mortality rate of 60 to 70 %. The incidence of Type 2 Diabetes is increasing all over the world and becoming a pandemic. But India remains the biggest contributor to global community.

II. Aims And Objectives
- To study the prevalence of asymptomatic coronary artery disease in Type 2 Diabetic mellitus patients by Tread Mill Test (TMT).
- To evaluate the positive correlation between TMT positive patients and raised hsCRP levels in asymptomatic diabetic population.
- To improve the long term survival in type2 diabetic patients by early detection of asymptomatic CAD and timely intervention.

III. Materials And Methods

Study Population
This study was conducted in 100 patients with Type 2 Diabetes patients visiting Diabetology clinic during the study period at Government Rajaji Hospital, Madurai.

Inclusion Criteria
1. All Type 2 Diabetes patients as defined by ADA.
2. Age >40 yrs.
3. Duration of Diabetes >5yrs.
4. Family history of CAD
5. Hypertension
6. Dyslipidemia
7. Current Tobacco smoking.
8. BMI >23 kg/m2
9. hsCRP levels
10. Patients with normal ECG and Echocardiogram

Exclusion Criteria
1. Previous history of CAD/undergone coronary intervention.
2. Patients with abnormal ECG and Echocardiogram suggestive of ischemia.
3. Patient Refusal to give consent.
4. Age <40 yrs.
5. Recently discovered Diabetes and Type 1 Diabetes
7. Patients with Chronic inflammatory condition
Anticipated Outcome
Screening of undiagnosed Coronary artery disease in Diabetes patients during asymptomatic period and improving outcome by taking timely intervention.

Data Collection
As per the previously designed, proforma will be used to collect clinical information of the samples and thorough clinical examination will be conducted. Electrocardiogram, Echocardiogram, Exercise treadmill test will be done. The levels of high sensitivity C reactive protein will be measured and correlate the data.

Investigations
1. Tread mill test (TMT)
2. Electrocardiogram
3. Echocardiogram
4. Fasting lipid profile
5. Fasting blood sugar
6. Post Prandial blood sugar
7. high sensitivity C-reactive protein.
8. serum Creatinine
9. complete urine analysis.

Design Of Study
Observational Study

Participants
100 patients attending Cardiology and Diabetology department at Govt Rajaji hospital, Madurai.

Analysis - Statistical analysis.

Conflict Of Interest . Nil
Financial Support . Nil

Data Collection
The previously formulated proforma used to collect the clinical and demographic details of the samples. Detailed history related to the present as well as a thorough history pertaining to other diseases were taken. Each patient was enquired about previous drug history, coronary artery disease, hypertension, diabetes and any other comorbid conditions.

A thorough clinical test and biochemical investigations were done to categorise the patients into diabetic with asymptomatic and associated risk factors for coronary artery disease. An Electrocardiography was recorded for all patients and they were subjected to Trans thoracic Echocardiography. Patients with normal ECG and ECHO will be undergoing to exercise treadmill test (TMT).

Laboratory Evaluation
1. Tread mill test (TMT)
2. Electrocardiogram
3. Echocardiogram
4. Fasting lipid profile
5. Fasting blood sugar
6. Post Prandial blood sugar
7. high sensitivity C-reactive protein.
8. serum Creatinine
9. complete urine analysis.

Electrocardiography
12 lead ECG was taken to all patients and screened for features suggestive of any ischemia or infarction.

Echo Cardiography
Transthoracic Echocardiography was done for all patients, looked for regional wall motion abnormalities. Patients with normal echocardiography will be segregated and will be subjected to exercise treadmill testing.
High Sensitivity C-Reactive Protein

Levels of High Sensitivity C-reactive protein will be measured in all patients who are subjected to treadmill testing by immuno turbidometric method.

History

Thorough history of CAD, chest pain, breathlessness, easy fatiguability, and syncopal attacks, previous hospitalisation have obtained.

Statistical Analysis

The data collected in the study was formulated into master chart in Microsoft office excel and statistical analysis was done with the help of computer by using SPSS software and sigma stat 3.5 version (2012). Using this software standard deviation, mean, percentage and p value were calculated through one way ANOVA, PEARSON correlation and Chi Square Test and \[ P \text{ value of } < 0.010 \] was taken as significant.

IV. Results And Interpretation

<p>| AGE DISTRIBUTION OF STUDY POPULATION (n=100) |</p>
<table>
<thead>
<tr>
<th>AGE</th>
<th>NO. OF CASES</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-50</td>
<td>29</td>
</tr>
<tr>
<td>51-60</td>
<td>51</td>
</tr>
<tr>
<td>&gt;60</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age group</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-50</td>
<td>9</td>
<td>20</td>
</tr>
<tr>
<td>51-60</td>
<td>14</td>
<td>37</td>
</tr>
<tr>
<td>&gt;60</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>31</td>
<td>69</td>
</tr>
</tbody>
</table>

Correlation of treadmill test positivity with age.

In our study mean age is 51.14 (+/-) 10 years with minimum age of 40 years. Maximum age of 65 years.

Comments

1. 29% of cases between 40 to 50 years of age.
2. 20% of study population above 60 years of age.
3. 51% of cases between 50-60 years of age.
4. Prevalence of CAD is increases as age advances.

<p>| GENDER DISTRIBUTION OF STUDY POPULATION (N=100) |</p>
<table>
<thead>
<tr>
<th>SEX</th>
<th>NO OF CASES</th>
</tr>
</thead>
<tbody>
<tr>
<td>MALE</td>
<td>72</td>
</tr>
<tr>
<td>FEMALE</td>
<td>28</td>
</tr>
</tbody>
</table>

Majority of study population were males (72%) while the remaining (28%) were females.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>25</td>
<td>47</td>
</tr>
<tr>
<td>Female</td>
<td>6</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>31</td>
<td>69</td>
</tr>
<tr>
<td>[ P \text{ value of } 0.009 ]</td>
<td>Significant</td>
<td></td>
</tr>
</tbody>
</table>

Comments:

1. Prevalence of CAD in diabetes patients is most commonly affecting the males than females.
2. In this study 32 to 35% of the male population positive for treadmill testing and is found to have asymptomatic coronary artery disease and statistically significant.
3. The prevalence of CAD is about 6% in females.

Table 3. Distribution Of Duration Of Diabetessamong StudyPopulation (100).

<table>
<thead>
<tr>
<th>DURATION OF DM</th>
<th>NO. OF CASES</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>24</td>
</tr>
<tr>
<td>5-10</td>
<td>57</td>
</tr>
<tr>
<td>&gt;10</td>
<td>19</td>
</tr>
</tbody>
</table>
Correlation of TMT positivity with duration of diabetes

<table>
<thead>
<tr>
<th>Duration of DM</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5</td>
<td>8</td>
<td>16</td>
</tr>
<tr>
<td>5-10</td>
<td>17</td>
<td>40</td>
</tr>
<tr>
<td>&gt; 10</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>31</td>
<td>69</td>
</tr>
</tbody>
</table>

Comments:
1. Among the study population 24% of cases are having less than 5 years of duration of diabetes.
2. 19% of cases more than 10 years of duration of diabetes.
3. 57% of cases between 5-10 years of duration of diabetes.
4. The prevalence of asymptomatic CAD 33% in the population group with duration of diabetes is >10 yrs.

Table 4. Distribution of hypertension among study population

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>45</td>
<td>27</td>
</tr>
<tr>
<td>Female</td>
<td>20</td>
<td>08</td>
</tr>
<tr>
<td>Total</td>
<td>65</td>
<td>35</td>
</tr>
</tbody>
</table>

Distribution of hypertension vs CAD risk among study population

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>29</td>
<td>13</td>
</tr>
<tr>
<td>No</td>
<td>2</td>
<td>56</td>
</tr>
<tr>
<td>Total</td>
<td>31</td>
<td>69</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.001</td>
<td>significant</td>
</tr>
</tbody>
</table>

Comments:
1. 65% of population group is hypertensive and majority of them are male population.
2. The risk of CAD is 29% among the diabetics with hypertension which is statistically significant.
3. Hence hypertension plays key risk factor for CAD in diabetes patients even though they are asymptomatic.

Table 5. Distribution of smoking among study population

<table>
<thead>
<tr>
<th>Smoking</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>40</td>
<td>32</td>
</tr>
<tr>
<td>Female</td>
<td>0</td>
<td>28</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>60</td>
</tr>
</tbody>
</table>

Table 6. Distribution of smoking and CAD risk among study population by TMT testing

<table>
<thead>
<tr>
<th>Smokers</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>23</td>
<td>10</td>
</tr>
<tr>
<td>No</td>
<td>8</td>
<td>59</td>
</tr>
<tr>
<td>Total</td>
<td>31</td>
<td>69</td>
</tr>
<tr>
<td>P value</td>
<td>0.004</td>
<td>Significant</td>
</tr>
</tbody>
</table>

Comments: The major population of smoking among study population is males and the prevalence of coronary artery disease among smokers is 65%. Hence the smoking plays an important risk factor for CAD in diabetic population.

Table 7. Distribution of HsCRP among study population (100).
The levels of hsCRP has been measured all patients in the study group and compared with among the patients with TMT positive and TMT negative population.

<table>
<thead>
<tr>
<th>Hs-crp</th>
<th>&lt;3 mg/l</th>
<th>&gt;3 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of cases</td>
<td>69</td>
<td>31</td>
</tr>
</tbody>
</table>

Distribution hsCRP mean vs CAD risk among study population

<table>
<thead>
<tr>
<th>CRP</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 3</td>
<td>2</td>
<td>69</td>
</tr>
<tr>
<td>&gt; 3</td>
<td>29</td>
<td>0</td>
</tr>
<tr>
<td>Mean</td>
<td>4.71</td>
<td>1.72</td>
</tr>
<tr>
<td>SD</td>
<td>1.21</td>
<td>0.157</td>
</tr>
<tr>
<td>p value</td>
<td>&lt; 0.001</td>
<td>Significant</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CRP</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>4.71</td>
<td>1.72</td>
</tr>
</tbody>
</table>
Comments:
1. The levels of hscrp is with value of >3 mg/l increased in patients with all cases of TMT positivity with mean value of 4.71mg/l and with standard deviation of 1.21 which is statistically significant.
2. The levels of Hscrp in patients with TMT negativity is < 3mg/l with mean value of 1.76mg/l which is mild to moderate elevation. Hence the levels of hscrp of >3mg/l can be considered as supportive marker Of CAD in asymptomatic type 2 diabetes patients and helps in prediction of future coronary event.

Limitations Of The Study
1. Sample size is small.
2. The study population involved patients seeking medical care in our hospital which is a tertiary care center and hence they may not represent the general population.
3. Patients with osteo arthritis and any deformities in lower limb can not undergo exercise test.
4. Patients may develop sudden MI during test so keen observation needed.
5. ICU and good cardiac care must be available before doing TMT. Because any time patient may collapse.
6. It is just a screening tool and further invasive procedure may be needed.

V. Discussion
The study was conducted in patients who attended diabetology clinic, at Govt Rajaji hospital, Madurai. Diagnosis of Diabetes Mellitus was made according to AMERICAN DIABETES ASSOCIATION, STANDARDS OF MEDICAL CARE IN DIABETES-2016. CAD risk is assessed according to ACC/AHA guidelines. Only newly diagnosed asymptomatic diabetic patients are taken in this study. After applying exclusion criteria 100 patients are selected for study.

Out of 100 patients 72 patients were male and 28 patients were female. It is consistent with previous clinical studies because nature of disease is more commonly seen in male when compared to females.

Out of 100 patients 24 patients were 5 yrs or less than 5 years duration of diabetes, 57 patients were 5-10 years of duration of diabetes and 19 patients were >10 years of duration of diabetes. Number of positivity is high among the group with between 5-10 years duration of diabetes.

AK Agarwal et al., have done similar study with 78 patients. but they divided patients into two groups with having non CAD group and CAD group. Among them 28% (22 patients) having subclinical ischemia in CAD group which is supported by TMT positivity. But in our study among 100 study population patients are purely non CAD group that is, asymptomatic and 31 patients (31%) having silent ischemia which is supported by TMT positivity alone, even though ECG and ECHO are showing no abnormalities.

Mee Kyoung, Ki ho song et al., have conducted the same study based on parameter of duration of diabetes with 213 patients. They found that Patients with more than 10 years of duration of diabetes are having significant correlation of coronary artery disease. Out of 213 patients 42% found to have positive treadmill test.

In this study patients showing positive TMT even with 5-10 years of duration which is consistent with that study and significant proportion of diabetics(31%) having silent ischemia which was detected by TMT.

Mee Kyoung Kim has selected the diabetics with age more than 60 and in our study we have taken more than 40 years of age. so this study detecting ischemia young diabetics than previous studies. hence we can decrease the diabetes related mortality and morbidity and improve the quality of life of diabetic patients.

Won Sang Yoo et al., have conducted a study with 115 diabetics. They are conducted the study with 2 groups: divided into group A (>2 risk factor), group B with (<1 risk factor). Patients are diagnosed to have diabetes by oral glucose tolerance test (OGTT). TMT was done according to Bruce protocol using 12 lead ECG.

This study found that Type 2 DM patients had a greater risk for CAD if they are older age group with longer duration of diabetes And Positive family history of CVD even though they were asymptomatic. Based on these results they recommended that TMT to be performed in order to detect CVD in these asymptomatic group. But in our study, we have conducted patients with risk factors like hypertension, smoking, long duration of diabetes and age of patients and some patients with pure diabetics were selected and subjected to TMT study.

In our study we found out that prevalence of asymptomatic CAD is more in patient group which is associated with cardiovascular risk factors such as hypertension, smokers, long duration of diabetes, male gender and advanced age.

Hae chong geong et al., conducted study with 445 diabetes patients with for detection of subclinical atherosclerosis patients using TMT, MDCT and HsCRP and found that prevalence of CAD in that group is 49% and the all the patients with TMT positivity are having the hscrp levels of 1+_7 mg/l.
In our study we have measured the hscrp levels in all 100 diabetes patients without any symptoms of CAD and finally found that the levels of hscrp elevated with reference range of >3 mg/l in those patients with TMT positivity.

Hence this study concludes that levels of Hscrp is elevated in type 2 diabetes patients with underlying CAD even though they are clinically asymptomatic and this can be used as supportive marker for detection of underlying CAD in patients with type2 diabetes patient.

VI. Summary

This observational prospective study was performed to identify the prevalence of asymptomatic atherosclerotic coronary artery disease in type 2 diabetes patients by using tread mill test as a screening tool and high sensitivity c-reactive protein as supportive marker.

100 patients were selected and they were evaluated on clinical and laboratory parameters after getting clearance from an institutional ethical committee with an informed consent. The data were entered in Microsoft Excel spread sheet and analysed statistically.

Prevalence of inducible ischemia is commonly seen in type 2 diabetes patients with associated cardiovascular risk factors even in the absence of symptoms and its high in patients with hypertension, smokers, and long duration of diabetes more than 5 to 10 years and advanced age and the levels of high sensitivity c-reactive protein is elevated in with range of >3 to 7 mg/l.

The risk is significantly high as duration of diabetes increases and since diabetes mellitus is a coronary equalant .Strict glycemic control and duration of disease is found to play important key factors in the prevalence of coronary artery disease in these patients.

VII. Conclusion

Early detection of asymptomatic coronary artery disease in type 2 diabetes mellitus has got paramount importance since CAD responsible for high mortality and morbidity.

TREAD MILL TESTING can be used as significant tool for detection of underlying CAD and it is supported by levels of HIGH SENSITIVITY C REACTIVE PROTEIN as surrogate marker.

The early introduction of medical intervention will reduce the disease related morbidity and mortality significantly.

By controlling hypertension, cessation of smoking, strict control blood sugar and avoidance of physical inactivity can reduce risk of CAD.

By all these measures we can improve long term survival of diabetic patients by timely intervention and follow up.

References


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Bhaskara” Screening of Asymptomatic Coronary Artery Disease in Type 2 Diabetes patients by TMT and it’s correlation with High Sensitivity C-Reactive Protein” IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 18, no. 9, 2019, pp 79-85.

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