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# Copeptin and coronary artery disease-Is there any association? A case-control study

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**Abstract**

**Background:** CAD is the most common heart disease. It can describe asymptomatic atherosclerosis, stable angina, and acute coronary syndrome (unstable angina, NSTEMI, STEMI). Multifactorial CAD. Modifiable and non-modifiable etiologic factors exist. Gender, age, family history, and genetics are unchangeable. Smoking, obesity, cholesterol levels, and psychosocial factors are modifiable.

**Methods:** Institutional Ethics Committee approved the prospective observational case-control study (Regd. No. ECR/84/Inst/OR/2013/RR-20). The Department of Cardiology at S.C.B Medical College and Hospital, Cuttack, comprised 80 CAD outpatients or inpatients between 2020 and 2022. Controls were age- and sex-matched. Patients with acute or chronic kidney illness, traumatic heart disease, head injury, morbidity, or refusal were eliminated.

**Results:** FBS, cholesterol, HDL, LDL, total and direct bilirubin, SGOT, SGPT, and alkaline phosphatase differed between groups ($P<0.05$). 56.25 percent had severe CAD and30 percent mild. Cases have greater copeptin than controls ($P<0.0001$). ROC curve analysis found a cut-off value of 0.98 and sensitivity and specificity of 83.8% and 76.2%. **Conclusion:** In contrast to healthy controls, CAD patients had greater copeptin levels, according to our study. Inthese cases, copeptin levels can be employed as a biomarker.

**Keyword:** CAD, FBS, COPEPTIN

## Background

Coronary artery disease (CAD) is the most common form of heart disease. It is used to describea range of clinical disorders from asymptomatic atherosclerosis and stable angina to acute coronary syndrome (unstable angina, NSTEMI, STEMI).[1]

CAD is a multifactorial phenomenon. Etiologic factors can be broadly categorized into non- modifiable and modifiable factors. Non-modifiable factors include gender, age, family history, and genetics. Modifiable risk factors include smoking, obesity, lipid levels, and psychosocial variables.[2] The conventional risk factors such as hypertension, diabetes mellitus dyslipidemia,smoking, and obesity are believed to be associated with increased prevalence of CAD in Indians.[3]

CAD is very common in both developed and developing worlds. In India in 2016, CVDs contributed to 28·1% of total deaths and 14·1% of total disability-adjusted life years (DALYs)compared with 15·2% and

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6·9%, respectively in 1990.[4] Within India, the rates of CAD vary markedly with highest in states of Kerala, Punjab and Tamil Nadu. Moreover, these states alsohave the highest prevalence of raised cholesterol levels and blood pressure. At present, India has the highest burden of acute coronary syndrome and ST-elevation myocardial infarction (MI).[3]

Symptoms of coronary artery disease presentations can vary from asymptomatic, stable chest pain (stable angina), and acute coronary syndrome (unstable angina, NSTEMI, and STEMI) to sudden cardiac death. Chest pain seen with stable angina is often mid-sternal, squeezing in quality, associated with a feeling of constriction or anxiety, radiating to the arms, neck, jaw, backor upper abdomen.

Over the past two decades, the introduction of multiple biomarkers has changed the landscape of cardiovascular diseases, especially in the management of patients with acute coronary syndromes (ACS) and heart failure (HF). Biomarkers can provide useful information for diagnostic, prognostic, and therapeutic strategies. Multiple biomarkers – including myoglobin, creatine phosphokinase (CPK) and CPK-MB – have been used in the past, but their delayed release after myocardial necrosis and/or their lack of specificity render them poorly exploitable in clinical practice and compromise their diagnostic performance.

Currently, troponin assessment is the gold standard for the early detection of myocardial infarction (MI) and this has shown better aptitude (sensitivity, specificity, early detection) compared to older biomarkers. However, conventional troponin elevation usually still occursrelatively late (3–6 hours) after ACS onset, and multiple samplings are often required and recommended in those patients who present early (within 3 hours) after chest pain onset (CPO).[5]

Copeptin has first been studied in order to investigate its prognostic potential in ACS. In patients presenting with MI, copeptin has been shown to be a strong predictor of worse outcome and a prognostic marker of death.[6] Of note, its relevance was increased when used in combination with other biomarkers (NT-proBNP and troponins).[7] A recent study reported that it may be beneficial to use conventional scoring systems and serum copeptin levels.[8] However, there is lack of information available in Indian subset of population. Hence, the present study was aimedto evaluate the diagnostic values of copeptin in CAD.

**Methods**

The prospective observational case-control study was approved by Institutional Ethics Committee (Regd. No. ECR/84/Inst/OR/2013/RR-20). Eighty diagnosed outpatients or in- patients of CAD within a period of two years between 2020 and 2022 at the Department of Cardiology at S.C.B Medical College and Hospital, Cuttack, were included. Similar number ofage- and sex-matched controls were included. The patients with acute or chronic kidney disease, traumatic heart disease, with a history of head injury, morbidly sick patients, or thoserefused to participate were excluded.

The patients' demographic and clinical characteristics were noted on a predesigned proforma. Severity of CAD was assessed using Gensini score.

***Laboratory investigations***

Routine biochemical parameters such as fasting plasma glucose, Liver Function Tests, serumlipid profile, serum urea and creatinine were done by auto analyzer (Toshiba and CANON TBA120FR) using standard commercial kits, adapted to auto analyzer at the Regional Diagnostic Centre (Biochemical Section), S.C.B Medical College and Hospital, Cuttack.

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Copeptin levels were determined using Abbkine Copeptin ELISA Kit.

***Statistical analysis***

Data were recorded in Microsoft® excel workbook 2019, and exported into SPSS v21.0 (IBM, USA) for statistical analysis. Quantitative normative variables were presented as mean, standard deviation, and compared using independent t-test. Categorical variables were compared using Chi square test. Quantitative non-normative variables were presented as median, Q1, Q3, and compared using Mann Whitney U test. ROC curve analysis was performed to calculate sensitivity and specificity. $P<0.05$ was considered significant.

**Results**

***Baseline characteristics***

Table 1 shows baseline characteristics of the study subjects. There was no significant differenceof age and sex between both groups. Cases have significantly higher BMI compared with controls ($P<0.00001$).

***Laboratory investigations***

Our study observed that FBS, cholesterol, HDL, LDL, total and direct bilirubin, SGOT, SGPT, and alkaline phosphatase were significantly different between both groups ($P<0.05$) (Table 2).

***Severity of CAD***

More than half of the patients had severe CAD (56.25%) followed by 30% with moderate disease (Figure 1).

***Copeptin levels***

Our study observed that there were a significantly higher copeptin levels in cases compared to controls ($P<0.0001$) (Figure 2). ROC curve analysis showed area under the curve of 0.901 with sensitivity and specificity of 83.8% and 76.2% respectively a cut-off value of 0.98 (Figure 3).

**Discussion**

Our study has shown that, in patients with CAD, there were significantly higher levels of copeptin. Copeptin have been associated with high mortality in patients with suspected acute coronary syndrome at hospital arrival in many previous studies. Balmelli et al.[9] found that highlevels of copeptin measured at hospital arrival were associated with worse prognosis: higher hospital mortality and 1-year mortality, in their prospective study in patients presenting to the Emergency Department with symptoms suggestive of acute MI of less than 12 h; although, in

this study, only 15.9% of patients were finally diagnoses of acute MI, being the other diagnoses unstable angina (14.0%), cardiac but noncoronary cause in 13.0%, noncardiac cause of chest pain in 48.4% and remained of unknown origin in 48.4% of patients included in the study. Maiselet al.[10] also found that high levels of copeptin were a powerful predictor of death at 180 days and hospitalization, in patients who arrived at hospital with chest pain within 6 h of pain onset; however, in this study the proportion of patients with acute MI was only 7.9%.

Lattuca et al.[11] measured level of copeptin and cardiac troponin I at the beginning of percutaneous coronary intervention in unselected patients with acute ST-segment elevation myocardial infarction. They found that levels of copeptin were higher in patients who died during hospitalization, during the first 30 days after the myocardial infarction and at 1 year follow-up; performed a multivariate analysis associating one year mortality with the presence cardiogenic shock, increasing age, the presence of higher levels of copeptin (> 128.2 pmol/L) and radial access.

In our study, ROC curve analysis showed area under the curve of 0.901 with sensitivity and specificity of 83.8% and 76.2% respectively a cut-off value of 0.98. A meta-analysis evaluated the prognostic

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value of copeptin in patients with acute coronary syndrome and concluded that elevated copeptin was associated with higher mortality with a pooled sensitivity of 0.77% (95% CI: 0.59–0.89) and a pooled specificity of 0.60 (95% CI: 0.47–0.71).[12]

Our study has various limitations. We did not evaluate the impact of time of the levels of copeptin levels. Secondly, we did not determine if the copeptin levels were associated with the worse outcomes. Lastly, we did not follow-up the patients.

**Conclusion**

Our study found a higher copeptin levels in CAD patients compared with healthy controls.

Copeptin levels can be used as a biomarker in these patients.

Table 1. Baseline characteristics

| | Controls (n=80) | Cases (n=80) | P value |
|---|---|---|---|
| Age (years) | 40.36±11.09 | 43.19±18.09 | 0.518 |
| Male sex, n(%) | 44 (55%) | 48 (60%) | 0.913 |
| BMI ($Kg/m^2$) | 24.12±1.38 | 26.99±3.76 | <0.0001 |

Data expressed as mean ± SD otherwise mentioned.Table

2: Laboratory characteristics

| | Controls (n=80) | Cases (n=80) | P value |
|---|---|---|---|
| FBS | 104.8±21.09 | 156.95±70.25 | <0.0001 |
| Sr. Chol. | 177.31±41.7 | 202.71±64.8 | 0.004 |
| Sr. TGL | 123.59±47.77 | 131.6±42.7 | 0.265 |
| Sr. HDL | 46.55±6.74 | 41.53±9.86 | <0.0001 |
| Sr. LDL | 110.81±39.4 | 129.95±19.3 | <0.0001 |
| Sr. VLDL | 23.64±10.37 | 26.06±8.62 | 0.110 |
| Sr. Urea | 23.63±7.58 | 23.96±7.3 | 0.775 |
| Sr. Creatinine | 0.8±0.17 | 0.86±0.27 | 0.087 |
| Bil (T), mg/dl | 0.57±0.23 | 0.85±0.53 | <0.0001 |
| Bil (D), mg/dl | 0.3±0.15 | 0.22±0.11 | <0.0001 |
| SGOT | 47.7±30.14 | 350.76±11.21 | <0.0001 |
| SGPT | 35.66±5.81 | 237.6±28.9 | <0.0001 |
| Alkaline Phosphatase | 220.7±52.51 | 282.8±94.42 | <0.0001 |

Data expressed as mean ± SD

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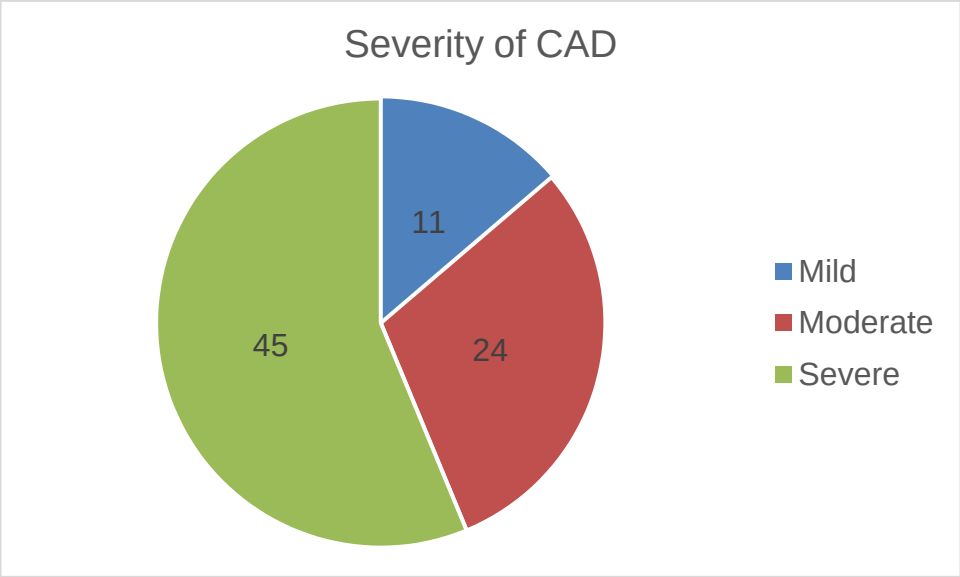


Figure 1. Severity of CAD

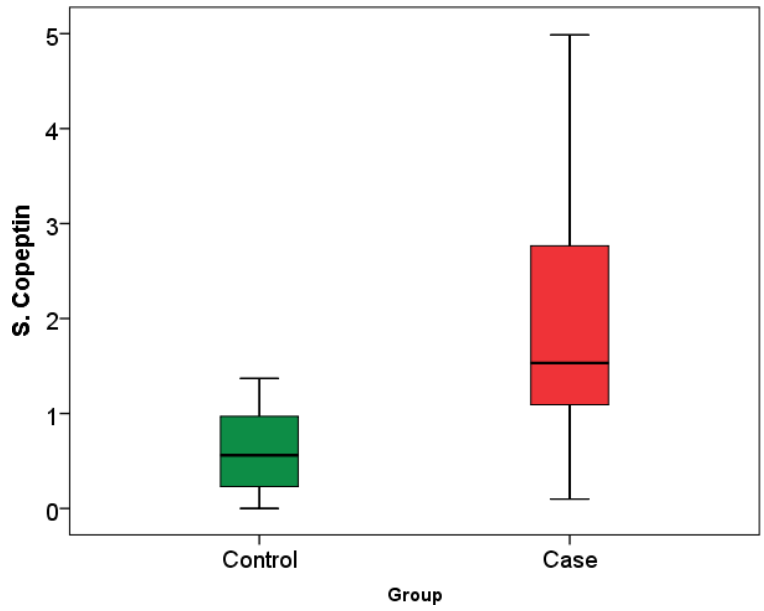


Figure 2. Box plot showing comparison of copeptin levels in control and case.

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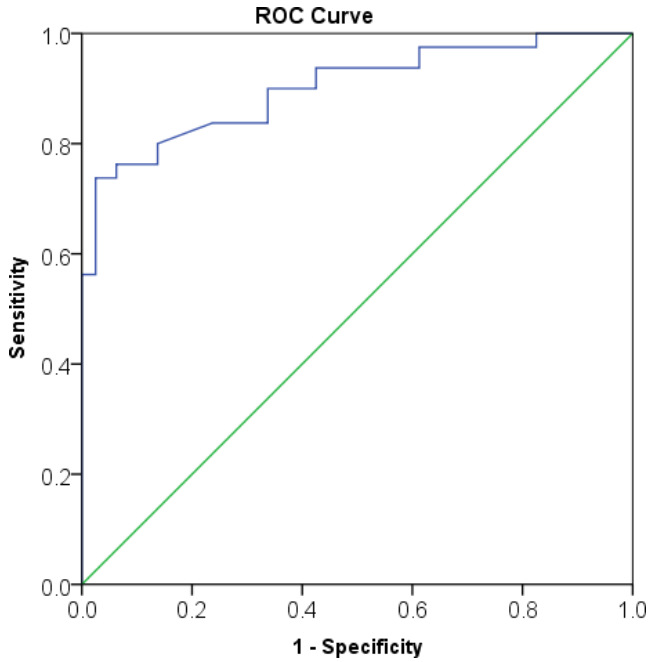


Figure 3: ROC curve showing area under the curve for copeptin levels between control andcases.

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