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**Original Research Article**

# Assessment of the Association between Bone Metabolic Markers and CAD Risk Score: An Observational Study

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**Conflict of interest: Nil**

**Abstract**

**Aim:** The aim of the present study to analyze the association between bone metabolic markers and CAD risk score in the general population of Bihar region.

**Material & Methods:** The present study was conducted at Department of Cardiology, Total 2000 participants were included in the study.

**Results:** There were 60% females and 40% males. Participants had co-morbidities like diabetes mellitus, dyslipidaemia, hypertension. The median Suita score was 43 points, and the median baPWV was 1,432 cm/s. TP1NP level was negatively associated with the CAD high-risk subgroup (Suita score ≥ 56) (odds ratio (OR) = 0.78, 95% confidence interval (CI) = 0.69–0.82, P < 0.001). There were significant differences in age, sex, history of smoking, history of diabetes, history of CAD, body mass index (BMI), SBP, DBP, baPWV, Suita score, total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, creatinine, uric acid, corrected calcium, phosphorus, hemoglobin, hemoglobin A1c, and N-terminal fragment of pro-B-type natriuretic peptide (NT-proBNP). Significant differences were observed in age, sex, smoking history, dyslipidemia history, hypertension history, BMI, SBP, DBP, baPWV, Suita score, total cholesterol, tri- glyceride, HDL cholesterol, LDL cholesterol, creatinine, eGFR, uric acid, corrected calcium, phosphorus, hemoglobin, and hemoglobin A1c. Significant differences were observed in age, sex, smoking history, diabetes history, hypertension history, CAD history, BMI, SBP, DBP, Suita score, total cholesterol, triglyceride, HDL cholesterol, LDL cholesterol, creatinine, uric acid, corrected calcium, phosphorus, hemoglobin, and hemoglobin A1c.

**Conclusion:** This study demonstrated that TP1NP levels decreased in participants with high Suita scores and high baPWV, suggesting that TP1NP down regulation may indicate future CAD risk and atherosclerosis progression in the general population of Bihar.

**Keywords:** Bone-type alkaline phosphatase, Brachial–ankle pulse wave velocity, cross-linked N-telopeptide of type 1 collagen, intact Parathyroid hormone, Suita score.



## Introduction

Chest pain is a common complaint in emergency departments with causes that range from innocent muscle pain to life-threatening diseases. The most common serious cause of chest pain is acute coronary syndrome (ACS), which in the aftermath induces a remodeling process with both positive adaptation and scar healing, but also with a potential for development of heart failure (HF). [1]

Recently, the prevalence of coronary artery disease (CAD) has been rapidly increasing. [2] In addition, mortality due to CAD was more than twice that due to malignancy. [2] It has been reported that classical CAD risk factors, such as aging, smoking, alcohol consumption, menopause, and lack of exercise, promote bone loss and bone quality deterioration, and induce the progression of atherosclerosis, suggesting that there is a relationship between abnormal bone metabolism and the development of atherosclerosis. [3] It is a complex and long-lasting process in which multiple factors such as lipid profile, inflammation and extracellular matrix (ECM) remodelling contribute to the phenotype of the atherosclerotic plaque. Whether a plaque develops into a vulnerable one, with increased risk of atherothrombotic complications, largely depends on its phenotype. [4] The ECM remodelling process in the arterial wall involves the synthesis and breakdown of ECM proteins such as collagens, proteoglycans and elastin. [5] Excessive or uncontrolled ECM remodelling in CAD has been proposed by previous studies showing that ECM degrading

enzymes, such as matrix metalloproteinases (MMPs), are upregulated in rupture-prone plaques. [6,7,8] Also, circulating levels of MMPs, particularly MMP-9, have been shown to predict the risk of CAD. [9,10]

Type I collagen is the most abundant protein in the human body and expressed in numerous tissues including skin, bone, tendons and arteries. It consists of two identical polypeptide α1 chains (COL1α1) and one α2 chain resulting in a triple helix molecule. Procollagen is the precursor to mature collagen in tissues and has three major domains: an N-terminal procollagen domain, a central triple helical domain and a C-terminal pro-collagen domain. [11] During the collagen synthesis, the N-terminal and C-terminal pro-collagens are cleaved off from the central domain. These fragments, including the PRO-C1 (N-terminal pro-peptide of type I collagen) biomarker, can reflect the systemic synthesis of type I collagen when measured in plasma. [15] In atherosclerotic plaques, type I collagen comprises 60% of the total protein content and is the primary component of the fibrous cap. [12,13] The type I collagen content is associated with a stable plaque phenotype. Reversibly, reduced synthesis and/or increased degradation of type I collagen may lead to thinning of the fibrous cap and thereby increase the risk of plaque rupture. [7,14,15] In line with this, circulating markers of collagen type I degradation have been shown to predict incident CAD. [16,17]

Constituent bone cells, such as osteocytes and osteoblasts, secrete osteocalcin and fibroblast growth factors, which were shown to affect atherosclerosis progression and carbohydrate metabolism. [18] In addition, the increased calcium and phosphorus release from bone associated with bone resorption was thought to cause vascular calcification and promote atherosclerosis. [19] An abnormal bone metabolism may play an essential role in the development of atherosclerosis. Bone metabolic turnover could be assessed by measuring bone formation markers (bone-type alkaline phosphatase [BAP], total N-terminal propeptide of type I collagen [TP1NP]), and bone resorption markers (cross-linked N-telopeptide of type 1 collagen [NTX]) in blood. [20] Therefore, this study aimed to identify the relationship between bone metabolic markers and CAD risk on the basis of the Suita score in the population of Bihar.

## Material & Methods

The present study was conducted at Department of Cardiology, NMCH, Sasaram, Rohtas, Bihar, India for two years. Total 2000 participants were included in the study. Participants with osteoporosis, chronic kidney disease, malignant disease, or primary wasting disease were excluded from the study. The present study measured the levels of circulating bone metabolic markers, including total type I collagen N-terminal propeptide (TP1NP), bone-type alkaline phosphatase, cross-linked N-telopeptide of type 1 collagen (NTX), and intact parathyroid hormone. CAD risk and atherosclerosis were evaluated using the Suita score and brachial– ankle pulse wave velocity (baPWV) measurement, respectively.

**Inclusion Criteria:** Participants (over 20 years old) who were living in Bihar

**Exclusion Criteria:** Participants who had osteoporosis, chronic kidney disease (CKD), any malignancy, primary wasting disease, or data deficiency were excluded from the present analysis.

### Methodology

In this cohort, young adult mean (YAM) and bone metabolism markers were measured in 1000 participants. Data on sociodemographic factors and lifestyle, including smoking and medical histories of stroke or CAD, were collected using self-administered questionnaires. Experienced physicians or nurses registered age and gender as well as measured their height, weight, blood pressure, and heart rate and performed physiological tests, such as electrocardiography. Fasting and non-fasting blood samples were collected from participants. BP, HbA1c and lipid profile will be recorded

### Measurements of Bone Metabolic Makers

Samples were centrifuged, and the upper serum phases were collected and frozen at − 80 ◦C before the assays. Serum samples from participants were used to measure TP1NP, BAP, NTX, and intact parathyroid hormone (PTH int) levels. Serum levels of TP1NP were measured by electrochemiluminescence immunoassay using a Cobas e 411 analyzer (Roche Diagnostics K.K., Tokyo, Japan). The detectable range of the TP1NP assay was 5 to 1200 ng/ml. Serum BAP level was determined using an enzyme-linked immunosorbent assay kit (Immunodiagnostic Systems, Tyne & Wear, UK) with a detection sensitivity of 1.0 μg/l. PTH level was measured using an intact assay using a chemiluminescent method (Abbott i2000, TX, USA). The lower detection threshold of the PTH int assay was 1 pg/ml. Serum NTX levels were determined by a fully automated enzyme-linked immunosorbent assay (ELISA) using Osteomark NTx Serum ELISA Test Kits (Alere Inc., Seattle, WA).

### Evaluating the Estimated Risk of CAD

The estimated CAD risk was calculated using the Suita score. [21] The Suita score includes age, sex, smoking history, blood pressure, LDL cholesterol, high-density lipoprotein (HDL) cholesterol, impaired glucose tolerance, and CKD stage.

Participants with a total score of 56 or higher were defined as high risk for CAD because they had a predicted probability of CAD of 9 % or higher at 10 years. It has been reported that the Suita score was more sensitive than the Framingham score in calculating the risk of CAD in the population of bihar. [22]

**Physiological Examinations**

Bilateral brachial–ankle pulse wave velocity (baPWV) was evaluated by utilizing BP-203RPE III (Omron Corporation, Kyoto, Japan). The details of the device and its use were explained, and its clinical relevance and good reproducibility were confirmed. [23] All examinations were performed by specially trained physicians and nurses. The cut-off value for baPWV was set at > 1,400 cm/s. We measured the YAM using dual-energy X-ray absorptiometry (DXA). [24]

Statistical analysis

Numerical variables are expressed as mean ± standard deviation in the case of normal distribution and median (interquartile range) in the case of skewed distribution. Categorical data are indicated in frequencies and percentages. The correlation between the two variables was assessed using Pearson's correlation coefficient. Binomial logistic regression analysis was performed to clarify the association between the Suita score high-risk group and each bone metabolic marker. The distribution of bone metabolic marker was classified by quartiles. The basic attributes were compared among the four groups using analysis of variance in the case of normal distribution and Kruskal–Wallis test in the case of skewed variables. Intergroup differences in demographic parameter proportions were examined using the chi-squared test. We performed a logistic regression analysis to identify the association between quartiles of TP1NP and factors associated with CAD high-risk and baPWV (>1,400 cm/s). All data were analyzed using IBM SPSS Statistics version 25 for Windows (IBM Corp., Armonk, NY, USA). Differences of $p < 0.05$ were considered to be statistically significant.

**Results**

**Table 1: Characteristics of analyzed participants**

| **Characteristics** | |
|---|---|
| Age | 59.5 ± 12.4 |
| Female, n (%) | 1200 (60) |
| Smoker, n (%) | 800 (40) |
| Diabetes mellitus, n (%) | 280 (14) |
| Dyslipidemia, n (%) | 680 (34) |
| Hypertension, n (%) | 560 (28) |
| Stroke, n (%) | 40 (2) |
| Coronary artery disease, n (%) | 42 (2.1) |
| BMIa (kg/m2) | 23.7±3.6 |
| Systolic BPb (mmHg) | 127.3±21.0 |
| Diastolic BPb (mmHg) | 76.6±12.8 |
| baPWVc (cm/s) | 1,432 (1,231–1,691) |
| Suita score, points | 43 (30–51) |
| Total cholesterol (U/L) | 209.0 ± 34.7 |
| Triglyceride (U/L) | 111.3 ± 71.6 |
| HDLd-cholesterol (U/L) | 62.8 ± 15.3 |
| LDLe-cholesterol (U/L) | 116.4 ± 29.3 |
| Creatinine (mg/dl) | 0.68 ± 0.15 |
| eGFRf (ml/min/1.73 m2) | 78.2 ± 15.2 |
| Uric acid (mg/dl) | 5.1 ± 1.4 |
| Corrected calcium (mg/dl) | 9.5 ± 0.3 |
| Phosphorus (mg/dl) | 3.5 ± 0.6 |
| Hemoglobin (g/dl) | 13.8 ± 1.5 |
| Hemoglobin A1c (%) | 5.5 ± 0.6 |
| NT-proBNPg (pg/mL) | 44 (27–73) |
| TP1NPh (ng/mL) | 43.9 (33.3–58.1) |
| BAPi (μg/L) | 12.1 (9.7–15.2) |
| NTXj (nM BCE/L) | 13.9 (11.6–16.9) |
| PTH intk (pg/mL) | 47 (38–57) |

There were 60% females and 40% males. Participants had co-morbidities like diabetes mellitus, dyslipidaemia, hypertension. The median Suita score was 43 points, and the median baPWV was 1,432 cm/s.

**Table 2: Association between Suita score (≥56 points) and bone metabolic markers, as estimated using a binomial logistic regression analysis**

| Variable | OR 95 %CI | P value |
|---|---|---|
| TP1NP (ng/mL) | 0.78 (0.69–0.82) | <0.001 |
| BAP (μg/L) | 1.10 (1.09–1.14) | <0.001 |
| NTXc (nM BCE/L) | 0.98 (0.97–1.01) | 0.412 |
| PTH intd (pg/mL) | 0.98 (0.98–0.99) | <0.001 |

TP1NP level was negatively associated with the CAD high-risk subgroup (Suita score ≥ 56) (odds ratio (OR) = 0.78, 95% confidence interval (CI) = 0.69–0.82, P < 0.001).

**Table 3: Characteristics of participants according to the quartiles of serum TP1NP levels**

| Parameter | Q1(<33.3) | Q2(33.3–43.8) | Q3(43.9–58.1) | Q4(<58.1) | P value |
|---|---|---|---|---|---|
| Number | 500 | 500 | 500 | 500 | |
| Age | 62.0 ± 12.8 | 57.3 ± 13.5 | 59.4 ± 12.0 | 59.5 ± 12.6 | <0.001 |
| Female, n (%) | 210 (42) | 255 (51) | 310 (62) | 375 (75) | <0.001 |
| Smoker, n (%) | 260 (52) | 225 (45) | 180 (36) | 140 (28) | <0.001 |
| Diabetes mellitus, n (%) | 100 (20) | 55 (11) | 50 (10) | 30 (6) | <0.001 |
| Dyslipidemia, n (%) | 175 (35) | 170 (34) | 180 (36) | 170 (34) | 0.580 |
| Hypertension, n (%) | 150 (30) | 130 (26) | 130 (26) | 120 (24) | 0.720 |
| Stroke, n (%) | 15 (3) | 10 (2) | 8 (1.6) | 9 (1.8) | 0.129 |
| Coronary artery disease, n (%) | 15 (3) | 10 (2) | 12 (2.4) | 4 (0.8) | 0.001 |
| BMIb (kg/m2) | 24.4 ± 3.6 | 23.7 ± 3.8 | 23.8 ± 3.9 | 23.6 ± 3.6 | <0.001 |
| Systolic BPc (mmHg) | 131.4 ± 18.5 | 129.0 ± 18.0 | 127.0 ± 17.0 | 125.5 ± 18.2 | <0.001 |
| Diastolic BPc (mmHg) | 76.4 ± 12.8 | 74.8 ± 11.6 | 75.3 ± 13.7 | 74.6 ± 12.6 | 0.003 |
| baPWV (cm/s) | 1,522(1,279–1,792) | 1,432(1,219–1,709) | 1,394(1,220–1,644) | 1,388(1,217–1,602) | <0.001 |
| Suita score, points | 48 (34–56) | 44 (29–52) | 42 (30–49) | 39 (30–46) | <0.001 |
| Total cholesterol (U/L) | 202.8 ± 35.5 | 207.3 ± 34.6 | 211.8 ± 32.0 | 213.4 ± 36.4 | <0.001 |
| Triglyceride (U/L) | 119.6 ± 80.2 | 114.6 ± 71.8 | 108.6 ± 72.5 | 98.4 ± 52.4 | <0.001 |
| HDLe-cholesterol (U/L) | 64.0 ± 15.5 | 62.5 ± 14.6 | 64.4 ± 14.6 | 64.0 ± 14.2 | <0.001 |
| LDLf-cholesterol (U/L) | 112.0 ± 28.4 | 116.4 ± 28.2 | 118.0 ± 28.6 | 119.5 ± 30.0 | <0.001 |
| Creatinine (mg/dl) | 0.74 ± 0.18 | 0.72 ± 0.16 | 0.68 ± 0.14 | 0.68 ± 0.12 | <0.001 |
| eGFRg (ml/min/1.73 m2) | 98.8 ± 24.0 | 98.2 ± 20.2 | 98.0 ± 18.2 | 96.4 ± 17.8 | 0.194 |
| Uric acid (mg/dl) | 5.4 ± 1.3 | 5.3 ± 1.3 | 5.1 ± 1.2 | 4.8 ± 1.2 | <0.001 |
| Corrected calcium (mg/dl) | 9.3 ± 0.4 | 9.3 ± 0.4 | 9.4 ± 0.4 | 9.4 ± 0.4 | 0.001 |
| Phosphorus (mg/dl) | 3.3 ± 0.4 | 3.4 ± 0.4 | 3.5 ± 0.4 | 3.6 ± 0.5 | 0.002 |
| Hemoglobin (g/dl) | 14.0 ± 1.5 | 13.9 ± 1.5 | 13.8 ± 1.4 | 13.6 ± 1.3 | <0.001 |
| Hemoglobin A1c (%) | 5.6 ± 0.70 | 5.5 ± 0.54 | 5.5 ± 0.51 | 5.4 ± 0.40 | <0.001 |
| NT-proBNP (pg/mL) | 47 (27–79) | 41 (24–69) | 43 (26–70) | 50 (29–74) | <0.001 |

There were significant differences in age, sex, history of smoking, history of diabetes, history of CAD, body mass index (BMI), SBP, DBP, baPWV, Suita score, total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, creatinine, uric acid, corrected calcium, phosphorus, hemoglobin, hemoglobin A1c, and N-terminal fragment of pro-B-type natriuretic peptide (NT-proBNP).

**Table 4: Characteristics of participants according to the quartiles of serum BAP levels**

| Parameter | Q1(<33.3) | Q2(33.3–43.8) | Q3(43.9–58.1) | Q4(<58.1 ) | P value |
|---|---|---|---|---|---|
| Number | 500 | 500 | 500 | 500 | |
| Age | 55.5 ± 12.6 | 57.4 ± 12.6 | 61.5 ± 12.8 | 62.8 ± 10.4 | <0.001 |
| Female, n (%) | 310 (62) | 255 (51) | 260 (52) | 320 (64) | <0.001 |
| Smoker, n (%) | 215 (43) | 210 (42) | 210 (42) | 175 (35) | <0.001 |
| Diabetes mellitus, n (%) | 50 (10) | 60 (12) | 65 (13) | 60 (12) | 0.212 |
| Dyslipidemia, n (%) | 150 (30.0) | 180 (36) | 175 (35) | 190 (38) | <0.001 |

| | | | | | |
|---|---|---|---|---|---|
| Hypertension, n (%) | 85 (17.0) | 130 (26) | 150 (30) | 160 (32) | <0.001 |
| Stroke, n (%) | 7 (1.4) | 13 (2.6) | 12 (2.4) | 12 (2.4) | 0.115 |
| Coronary artery disease, n (%) | 10 (2) | 12 (2.6) | 10 (2) | 10 (2) | 0.512 |
| BMIb (kg/m2) | 23.6 ± 3.6 | 23.7 ± 3.6 | 24.0 ± 3.7 | 24.0 ± 3.6 | <0.001 |
| Systolic BPc (mmHg) | 123.7 ± 18.8 | 128.2 ± 18.0 | 131.5 ± 18.4 | 132.8 ± 18.2 | <0.001 |
| Diastolic BPc (mmHg) | 74.6 ± 11.6 | 74.8 ± 11.1 | 76.4 ± 12.8 | 76.4 ± 11.7 | <0.001 |
| baPWV (cm/s) | 1,320(1,131–1,595) | 1432(1,231–1,685) | 1,455(1,277–1,741) | 1,488(1,305–1,726) | <0.001 |
| Suita score, points | 38 (22–49) | 41 (30–52) | 42 (34–52) | 43 (36–50) | <0.001 |
| Total cholesterol (U/L) | 205.7 ± 33.9 | 206.2 ± 34.6 | 209.7 ± 34.3 | 212.3 ± 35.6 | <0.001 |
| Triglyceride (U/L) | 103.0 ± 72.2 | 111.3 ± 75.3 | 110.7 ± 69.2 | 115.8 ± 69 | <0.001 |
| HDLe-cholesterol (U/L) | 65.2 ± 15.9 | 62.5 ± 14.7 | 62.1 ± 15.2 | 62.0 ± 15.1 | <0.001 |
| LDLf-cholesterol (U/L) | 112.4 ± 28.1 | 116.3 ± 29.7 | 117.7 ± 29.4 | 119.0 ± 29.7 | <0.001 |
| Creatinine (mg/dl) | 0.69 ± 0.15 | 0.71 ± 0.15 | 0.70 ± 0.15 | 0.67 ± 0.14 | <0.001 |
| eGFRg (ml/min/1.73 m2) | 103.4 ± 22.4 | 97.8 ± 19.2 | 96.8 ± 18.8 | 94.5 ± 17.5 | <0.001 |
| Uric acid (mg/dl) | 5.0 ± 1.3 | 5.3 ± 1.3 | 5.3 ± 1.3 | 5.0 ± 1.2 | <0.001 |
| Corrected calcium (mg/dl) | 9.3 ± 0.4 | 9.4 ± 0.4 | 9.4 ± 0.3 | 9.4 ± 0.4 | <0.001 |
| Phosphorus (mg/dl) | 3.5 ± 0.4 | 3.4 ± 0.4 | 3.4 ± 0.5 | 3.5 ± 0.5 | 0.003 |
| Hemoglobin (g/dl) | 13.4 ± 1.4 | 13.9 ± 1.5 | 14.0 ± 1.4 | 14.1 ± 1.3 | <0.001 |
| Hemoglobin A1c (%) | 5.4 ± 0.50 | 5.5 ± 0.53 | 5.5 ± 0.57 | 5.5 ± 0.59 | <0.001 |
| NT-proBNP (pg/mL) | 45 (27–71) | 43.5 (25–75) | 43 (26–71) | 46 (27–76) | 0.300 |

Significant differences were observed in age, sex, smoking history, dyslipidemia history, hypertension history, BMI, SBP, DBP, baPWV, Suita score, total cholesterol, tri- glyceride, HDL cholesterol, LDL cholesterol, creatinine, eGFR, uric acid, corrected calcium, phosphorus, hemoglobin, and hemoglobin A1c.

**Table 5: Characteristics of participants according to the quartiles of serum PTH levels**

| **Parameter** | **Q1(<33.3)** | **Q2(33.3–43.8)** | **Q3(43.9–58.1)** | **Q4(<58.1 )** | **P value** |
|---|---|---|---|---|---|
| Number | 500 | 500 | 500 | 500 | |
| Age | 58.6 ± 12.6 | 57.6 ± 12.2 | 59.8 ± 12.2 | 58.8 ± 12.8 | <0.001 |
| Female, n (%) | 240 (48) | 290 (58) | 300 (60) | 310 (62) | <0.001 |
| Smoker, n (%) | 220 (44) | 200 (40) | 195 (39) | 195 (39) | 0.032 |
| Diabetes mellitus, n (%) | 80 (16) | 60 (12) | 50 (10) | 50 (10) | <0.001 |
| Dyslipidemia, n (%) | 190 (38) | 170 (34) | 160 (32) | 175 (35) | 0.088 |
| Hypertension, n (%) | 125 (25) | 110 (22) | 140 (28) | 155 (31) | <0.001 |
| Stroke, n (%) | 14 (2.8) | 10 (2) | 12 (2.4) | 9 (1.8) | 0.245 |
| Coronary artery disease, n (%) | 16 (3.2) | 9 (1.8) | 10 (2) | 8 (1.6) | 0.024 |
| BMIb (kg/m2) | 23.7 ± 3.5 | 23.6 ± 3.8 | 23.9 ± 3.7 | 24.6 ± 3.5 | <0.001 |
| Systolic BPc (mmHg) | 126.4 ± 18.2 | 125.5 ± 18.4 | 128.4 ± 18.4 | 131.2 ± 18.0 | <0.001 |
| Diastolic BPc (mmHg) | 72.8 ± 11.6 | 73.7 ± 11.1 | 75.2 ± 11.5 | 77.0 ± 12.1 | <0.001 |
| baPWV (cm/s) | 1,450(1,217–1,749) | 1,411(1,226–1,669) | 1,425(1,214–1,684) | 1,436(1,258–1,670) | 0.140 |
| Suita score, points | 43 (30–53) | 41 (30–50) | 41 (30–50) | 41 (30–49) | 0.001 |
| Total cholesterol (U/L) | 204.9 ± 35.0 | 207.8 ± 34.1 | 208.6 ± 34.6 | 210.4 ± 35.0 | 0.002 |
| Triglyceride (U/L) | 117.1 ± 76.0 | 107.4 ± 70.6 | 104.0 ± 66.1 | 113.2 ± 73.0 | <0.001 |
| HDLe-cholesterol (U/L) | 60.9 ± 15.0 | 63.3 ± 15.2 | 63.5 ± 15.4 | 63.9 ± 15.3 | <0.001 |
| LDLf-cholesterol (U/L) | 114.5 ± 29.1 | 116.0 ± 28.8 | 117.2 ± 29.1 | 117.8 ± 30.3 | 0.035 |
| Creatinine (mg/dl) | 0.71 ± 0.15 | 0.69 ± 0.15 | 0.69 ± 0.14 | 0.69 ± 0.15 | <0.001 |
| eGFRg (ml/min/1.73 m2) | 96.5 ± 20.0 | 99.3 ± 20.0 | 98.6 ± 19.2 | 98.1 ± 20.5 | 0.301 |
| Uric acid (mg/dl) | 5.2 ± 1.3 | 5.1 ± 1.3 | 5.1 ± 1.3 | 5.2 ± 1.3 | 0.035 |
| Corrected calcium (mg/dl) | 9.5 ± 0.4 | 9.4 ± 0.3 | 9.3 ± 0.3 | 9.3 ± 0.4 | <0.001 |
| Phosphorus (mg/dl) | 3.5 ± 0.5 | 3.5 ± 0.4 | 3.5 ± 0.4 | 3.3 ± 0.4 | <0.001 |
| Hemoglobin (g/dl) | 14.0 ± 1.4 | 13.8 ± 1.4 | 13.8 ± 1.4 | 13.8 ± 1.5 | 0.030 |
| Hemoglobin A1c (%) | 5.5 ± 0.62 | 5.5 ± 0.53 | 5.5 ± 0.54 | 5.5 ± 0.51 | 0.026 |
| NT-proBNP (pg/mL) | 43 (25–71) | 44 (27–70) | 46 (27–76) | 45 (26–76) | 0.240 |

Significant differences were observed in age, sex, smoking history, diabetes history, hypertension history, CAD history, BMI, SBP, DBP, Suita score, total cholesterol, triglyceride, HDL cholesterol,

LDL cholesterol, creatinine, uric acid, corrected calcium, phosphorus, hemoglobin, and hemoglobin A1c.

## Discussion

Cardiovascular disease is the leading cause of death and source of disease burden worldwide. Most clinical manifestations, such as coronary artery disease (CAD), are caused by atherosclerosis. [25] One of the indicators of atherosclerosis is bilateral brachial–ankle pulse wave velocity (baPWV), which has been used to predict cardiovascular disorders (CVDs) and subsequent prognosis. [26] Constituent bone cells, such as osteocytes and osteoblasts, secrete osteocalcin and fibroblast growth factors, which were shown to affect atherosclerosis progression and carbohydrate metabolism. [27]

There were 60% females and 40% males. Participants had co-morbidities like diabetes mellitus, dyslipidaemia, hypertension. The median Suita score was 43 points, and the median baPWV was 1,432 cm/s. TP1NP level was negatively associated with the CAD high-risk subgroup (Suita score ≥ 56) (odds ratio (OR) = 0.78, 95% confidence interval (CI) = 0.69–0.82, P < 0.001). There were significant differences in age, sex, history of smoking, history of diabetes, history of CAD, body mass index (BMI), SBP, DBP, baPWV, Suita score, total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, creatinine, uric acid, corrected calcium, phosphorus, hemoglobin, hemoglobin A1c, and N-terminal fragment of pro-B-type natriuretic peptide (NT-proBNP). Recently, bone metabolic markers in blood attracted attention as new biomarkers for developing CAD and life prognosis. [28] In this study, we compared the Suita score with bone metabolic markers as a predictive marker for CAD development. Logistic regression analysis showed that, among bone metabolic markers, circulating TP1NP level was negatively associated with Suita score high-risk group (≥56 points) and baPWV (>1,400 cm/s), suggesting that TP1NP levels among bone metabolic markers may be the strongest marker for future CAD risk. This study showed that low PTH int levels were associated with the Suita score high-risk group (≥56 points). Consistent with this study, a relationship between lower PTH and a high CAD risk has been reported in a previous study. [29] In addition, hypoparathyroidism might affect bone metabolism. [30] These observations speculated that low PTH int levels might be associated with the secretion of bone metabolic markers and may be one of the CAD risk factors.

Significant differences were observed in age, sex, smoking history, dyslipidemia history, hypertension history, BMI, SBP, DBP, baPWV, Suita score, total cholesterol, tri- glyceride, HDL cholesterol, LDL cholesterol, creatinine, eGFR, uric acid, corrected calcium, phosphorus, hemoglobin, and hemoglobin A1c. Significant differences were observed in age, sex, smoking history, diabetes history, hypertension history, CAD history, BMI, SBP, DBP, Suita score, total cholesterol, triglyceride, HDL cholesterol, LDL cholesterol, creatinine, uric acid, corrected calcium, phosphorus, hemoglobin, and hemoglobin A1c. In addition, reports that examined the association between bone metabolic markers and CVD showed a positive correlation. [31,32] Although these reports showed controversial results compared to that of the present study, these studies included elderly individuals and participants with osteoporosis. Indeed, circulating bone metabolic markers including TP1NP levels were affected by aging. [33-35] On the other hand, it has been reported that blood TP1NP levels are negatively correlated with traditional CVD risk factors, such as abnormal glucose metabolism and obesity. [36,37]

## Conclusion

The present study demonstrated that TP1NP levels decreased in participates with high Suita scores and high baPWV and suggested that downregulated TP1NP might indicate future CAD risk and atherosclerosis progression in the general Bihar population.

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