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Review

To Assess the Influence of Adiponectin Levels on Type 2 Diabetes Mellitus Among Myocardial Infarction Patients

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Abstract:

Introduction: Adiponectin, an adipokine with insulin-sensitizing properties, may play a key role in the metabolic trajectory following myocardial infarction. This longitudinal study investigated whether low baseline adiponectin levels predict new-onset Type 2 Diabetes Mellitus (T2DM) in STEMI survivors without prior diabetes. **Objective:** This longitudinal study aimed to evaluate the influence of baseline plasma adiponectin levels on the risk of developing new-onset Type 2 Diabetes Mellitus (T2DM) in ST-segment elevation myocardial infarction (STEMI) survivors without prior diabetes. **Methods:** We enrolled 540 non-diabetic patients treated with primary percutaneous coronary intervention (pPCI) at a tertiary care centre in Chennai. Baseline plasma adiponectin was measured using a validated assay. Participants were followed for two years via quarterly telephone interviews, with T2DM diagnosis confirmed via medical records. Cox proportional hazards regression, adjusted for confounders including HbA1c and waist circumference, was used to assess risk. **Results:** During follow-up, 24 participants developed T2DM. A strong inverse dose-response relationship was observed between adiponectin levels and T2DM risk. Compared to the highest adiponectin quartile (Q4), patients in the lowest quartile (Q1) had a more than four-fold higher unadjusted hazard ratio (HR 4.12, 95% CI 3.10–5.48), which remained significant after multivariable adjustment (adjusted HR 3.56, 95% CI 2.62–4.84, $p<0.001$). Higher baseline HbA1c was also an independent predictor (aHR 1.32 per %, 95% CI 1.15–1.51, $p<0.001$). **Conclusion:** Low circulating adiponectin is a powerful, independent predictor of new-onset T2DM in non-diabetic STEMI patients post-pPCI.

Keywords: Adiponectin, Type 2 Diabetes Mellitus, Myocardial Infarction, Primary Percutaneous Coronary Intervention, Longitudinal Study

Introduction

Cardiovascular diseases are the leading cause of mortality worldwide causing about 17.9 million deaths each year. Of which ST-segment elevated myocardial infarction (STEMI) is the most severe presentation of acute coronary syndrome.(1) Indians have what has been coined as the "Asian Indian Phenotype", where they tend to have greater visceral adiposity and lower adiponectin levels than the Caucasian counterparts though the Body Mass Index (BMI) is relatively low. Thus, making us more prone to premature coronary artery disease as well as metabolic syndrome.(2) Although advancements in medicine have allowed for aggressive management strategies such as primary percutaneous coronary intervention (pPCI), these patients have a high incidence of developing metabolic derangements secondary to their index

myocardial infarction (MI). Among them, Type 2 Diabetes Mellitus(T2DM) being the most prevalent secondary disease that is encountered which can negatively impact cardiovascular outcomes as well as increase chances of recurrence.(3)

Visceral fat is also now known to act as an endocrine tissue releasing so called "adipokines". These hormones act as cytokines which regulate inflammatory reactions as well as insulin resistance. Adiponectin, a collagen-like protein that is produced exclusively by adipocytes, is known to have anti-inflammatory, anti-atherogenic and insulin sensitizing properties. Adiponectin is unique from most other adipokines as it has been shown to have an inverse relationship with fat mass. (4) It achieves its actions through activation of AMP-activated protein kinase (AMPK).(4)

During STEMI, there is an abrupt inflammatory insult to the body followed by reperfusion injury. Adiponectin levels may become deranged during this period but has not been studied specifically for predicting new onset T2DM in STEMI patients who receive pPCI.(5) There are literatures that are extensively studying the correlation of C reactive protein (CRP) and Troponin-I as markers of tissue damage, but not much attention has been put on adiponectin levels at baseline as a predictor of metabolic derangements.

The change from an acute heart attack to a chronic metabolic condition is like getting hit twice for the patient. To give tailored care after myocardial infarction, you need to know what biomarkers come before this change. Since there is limited evidence directly associating decreased adiponectin levels with T2DM risk in post-MI populations, there is a distinct need for longitudinal studies that monitor these patients from the initial acute intervention to extended follow-up periods. Early identification of high-risk patients may provide targeted lifestyle or pharmacological therapies, potentially modifying the metabolic trajectory of STEMI survivors.

Objectives

- To estimate the baseline plasma adiponectin levels in ST-segment elevated Myocardial Infarction patients who underwent primary percutaneous coronary intervention.
- To assess the incidence of new-onset Type 2 Diabetes Mellitus over a two-year follow-up period in the study population and to determine the correlation between reduced adiponectin levels and the risk of developing Type 2 Diabetes Mellitus, and confounding factors like Body Mass Index and baseline inflammation.

Materials and Methods

Study Setting and Period

The study was performed at a major, multi-specialty tertiary care hospital in Chennai, which houses a dedicated cardiothoracic unit. The initial phase involved acquiring the medical records of relevant patients from the hospital database, covering a six-month period from April to September 2023. From these records, a potential study population was identified.

This group then underwent primary screening through structured telephone interviews conducted over the subsequent two months (October to November 2023). Individuals who met the predefined eligibility criteria during this screening were formally enrolled as participants.

Following enrolment, a long-term follow-up protocol was implemented. Each participant was contacted for a telephone interview once every three months, beginning in December 2023 and continuing through December 2025. This schedule resulted in a total of nine follow-up visits per participant, allowing for the longitudinal tracking of outcomes.

Finally, all data gathered from the screening and follow-up phases were compiled and statistically analyzed during a dedicated period from January to February 2026.

Sampling Procedure

A consecutive sampling method was employed. All STEMI patients treated with primary percutaneous coronary intervention (pPCI) at the hospital during the six-month data extraction period (April to September 2023) were considered for inclusion. This initial cohort was screened for eligibility via telephone. The final sample consisted of all eligible patients who provided consent and were available for the longitudinal follow-up phase of the study.

Study Population and Eligibility Criteria

The study participants were ST-segment elevation myocardial infarction (STEMI) patients treated with primary percutaneous coronary intervention (pPCI) at the hospital. Both male and female patients were included in the study and participants with age greater than fifty five years were included in the study. Patients with a prior diagnosis of diabetes were excluded.

Every year, the hospital does about 1,000 percutaneous coronary interventions. From these, we only looked at individuals who were suspected of having STEMI and were admitted within 12 hours after the start of chest pain that lasted at least thirty minutes. To be eligible for enrolment, there had to be a persistent ST-segment elevation of more than 2 mm in at least two adjacent precordial ECG leads, or more than 1 mm in at least two adjacent limb leads, or a new left bundle branch block. Patients having troponin levels more than 0.5 mg/L or those who did not necessitate pPCI due to the lack of blockage were excluded.

At first, 626 patients were found. According to the criteria for exclusion, 41 were not included. We couldn't get in touch with or keep an eye on 65 more patients, so they were left out. As a result, 540 STEMI patients were included in the study.

Study variables

The following baseline characteristics were recorded in the study – Age and gender of the patients, Body Mass Index (BMI), Smoking status, Blood glucose, C- Reactive Protein, Serum creatinine, eGFR and Serum cholesterol levels. Hypertension was defined as use of blood pressure–lowering drugs and hypercholesterolemia as treatment with cholesterol-lowering drugs at the time of interview. Multivessel disease was defined as two- or three-vessel disease.

Data collection procedure

All patients were followed for an average of two years and follow-up was 100% complete (n = 540). Diagnosis of Type 2 Diabetes Mellitus was obtained from hospital records of the patients through telephonic interview. All events found using telephonic interview were carefully cross validated through photographs of medical records (e.g., laboratory tests, medical charts, and hospital summaries), excluding possibly misclassified events.

The study was approved by the institutional ethics committee and informed consent was obtained from all participants. The data collection of the first visit was through face to face interview. Following visits were telephonic interviews.

During the initial visit, blood samples were collected from participants. These samples were immediately allocated into 4 mL EDTA-containing tubes to prevent coagulation. Within 30 minutes of collection, the samples were centrifuged at 10,000 RPM for 10 minutes to separate the plasma from the cellular components.

The resulting plasma was then aliquoted into Nunc cryogenic tubes and stored at –80°C to preserve the integrity of the analytes until analysis. All samples were subsequently analyzed in a blinded fashion by a dedicated core laboratory to ensure objective results.

Total plasma adiponectin levels were quantified using a validated, high-sensitivity in-house sandwich ELISA. To make sure of a comprehensive metabolic profile, the assay utilized monoclonal antibodies directed against epitopes which were conserved. This allowed for the simultaneous detection of all three major circulating isoforms which are low molecular weight (LMW) trimers, medium molecular weight (MMW) hexamers, and high molecular weight (HMW) multimers. For accuracy and precision, all samples were analyzed in duplicate. The assay has a detection limit of 1.5 mg/L, with intra-assay and inter-assay coefficients of variation reported at <5% and <7%, respectively.

In addition to adiponectin, other key biomarkers were measured. C-reactive protein (CRP), creatinine, and blood glucose levels were determined using the hospital's routine laboratory methods.

Finally, renal function was assessed by calculating the estimated glomerular filtration rate (eGFR). This was derived from the serum creatinine level, along with the patient's age and sex, using the standardized Modification of Diet in Renal Disease (MDRD) formula.

Statistical Analysis

The statistical analysis employed a range of appropriate tests to characterize the cohort and evaluate associations. The data were managed in Microsoft Excel and all analyses were performed using SPSS software, version 21. For the baseline characteristics in Table 1, continuous variables were described using mean ± standard deviation for normally distributed data and median [interquartile range] for skewed data (e.g., CRP, ALT, GGT). Categorical variables were presented as counts and percentages (%). In Table 2, participants were stratified into quartiles based on serum adiponectin levels. Differences in baseline characteristics across quartiles were tested using one-way ANOVA for normally distributed continuous variables (e.g., age, lipids, waist circumference), the Kruskal-Wallis test for non-normally distributed continuous variables

(e.g., CRP, ALT, GGT), and the chi-square test for categorical variables (e.g., hypertension, smoking status). The primary time-to-event outcome—development of Type 2 Diabetes Mellitus (T2DM)—was analyzed using Cox proportional hazards regression. Hazard ratios (HR) with 95% confidence intervals (CI) were calculated, initially in unadjusted models and then in a multivariable model adjusted for key covariates. The significance level for all statistical tests was set at a p-value of less than 0.05.

Results

This longitudinal study enrolled 540 STEMI patients without prior diabetes, who were treated with primary PCI at a tertiary hospital in Chennai. The primary exposure was baseline plasma adiponectin level, measured via a validated assay, and the main outcome was the subsequent development of Type 2 Diabetes Mellitus (T2DM), confirmed by medical records. A total of 24(participants developed Type 2 Diabetes Mellitus during the follow up period.

The Table 1 describes the baseline characteristics of a study participant with the mean age of 59.35 ± 9.77 years. The average HbA1c range was 5.95 ± 0.51%. The LDL was high with 116.05 ± 40.52 mg/dL and triglycerides 165.73 ± 36.57 mg/dL. The HDL was low with 40.38 ± 5.76 mg/dL, and CRP was 4.60 mg/L. Abdominal obesity is indicated by a high mean waist circumference of 112.83 ± 9.53 cm. Comorbidities are highly prevalent, with over half the participants having a history of hypertension (57.2%) or hypercholesterolemia (57.6%), and 15.9% having a previous myocardial infarction. Furthermore, 40.2% are current smokers.

Table 1: Baseline characteristics of the study participants (n=540)

Variable	Frequency (N)	Percentage (%)
Age (years)[a]	59.35 ± 9.77	
HbA1C (%)[a]	5.95 ± 0.51	
HDL Cholesterol (mg/dL) [a]	40.38 ± 5.76	
LDL Cholesterol (mg/dL) [a]	116.05 ± 40.52	
Triglycerides (mg/dL) [a]	165.73 ± 36.57	
Total Cholesterol (mg/dL) [a]	189.60 ± 39.67	
CRP (mg/L)[b]	4.60 [2.63–8.25]	
Waist Circumference (cm) [a]	112.83 ± 9.53	
Serum Uric Acid (mg/dL) [a]	6.92 ± 1.25	
ALT (U/L) [b]	33.72 [27.76–39.93]	
GGT (U/L) [b]	42.14 [36.03–51.34]	
Serum Creatinine (mg/dL) [a]	1.00 ± 0.29	
eGFR (MDRD) [a]	91.73 ± 179.62	
History of Hypertension	309	57.2
Current Smoker	217	40.2
Hypercholesterolemia	311	57.6
History of Previous MI	086	15.9

[a] Mean SD, [b] Median[IQR]

The Table 2 describes the association between baseline characteristics and Adiponectin levels. Participants were stratified into quartiles (Q1-Q4). Moving from the lowest (Q1) to the highest (Q4) quartile, there were marked, stepwise improvements: mean waist circumference decreased from 123.0 cm to 105.8 cm, mean HbA1c fell from 6.5% to 5.5%, and mean HDL cholesterol improved from 37.3 mg/dL to 42.8 mg/dL. Concurrently, mean triglycerides decreased substantially from 192.9 mg/dL to 145.2 mg/dL, and mean uric acid levels dropped from 7.9 mg/dL to 6.2 mg/dL. Liver enzymes also showed a favourable trend, with median ALT declining from 40.6 U/L to 29.1 U/L and median GGT from 52.1 U/L to 36.7 U/L ($p < 0.001$). Total cholesterol, LDL cholesterol, median CRP, and renal function showed no significant differences. The prevalence of hypertension varied significantly (61.8% in Q1; 47.4% in Q4, p=0.008), while other comorbidities and smoking status were similar across quartiles.

Table 2: Association between Type 2 Diabetes Mellitus and Adiponectin levels (n=540)

Variable	**Q1 (Lowest) (n=136)**	**Q2 (n=135)**	**Q3 (n=134)**	**Q4 (Highest) (n=135)**	**P-value**
Age (years)	59.5 ± 9.2	60.0 ± 10.4	58.9 ± 9.6	59.0 ± 9.9	0.833
Waist Circumference (cm)	123.0 ± 9.7	113.0 ± 6.0	109.3 ± 5.0	105.8 ± 5.7	<0.001
HbA1C (%)	6.5 ± 0.5	6.0 ± 0.3	5.8 ± 0.3	5.5 ± 0.3	<0.001
Total Cholesterol	190.6 ± 40.0	190.9 ± 38.9	190.7 ± 37.8	186.2 ± 41.8	0.599
HDL Cholesterol	37.3 ± 5.8	40.5 ± 5.5	41.0 ± 5.5	42.8 ± 4.9	<0.001
LDL Cholesterol	114.8 ± 39.4	116.5 ± 40.9	118.5 ± 39.2	114.4 ± 42.6	0.738
Triglycerides	192.9 ± 34.5	169.0 ± 30.7	155.5 ± 28.3	145.2 ± 32.0	<0.001
CRP (mg/L)	4.7 [2.6–10.4]	4.7 [2.7–7.7]	4.3 [2.6–7.8]	4.7 [2.9–7.3]	0.961
Uric Acid (mg/dL)	7.9 ± 1.3	6.9 ± 1.1	6.6 ± 1.0	6.2 ± 1.1	<0.001
ALT (U/L)	40.6 [35.3–46.0]	34.6 [27.9–39.5]	32.5 [27.0–36.7]	29.1 [24.2–34.3]	<0.001
GGT (U/L)	52.1 [44.7–60.5]	43.9 [39.2–49.8]	39.8 [34.4–43.8]	36.7 [29.4–44.3]	<0.001
Serum Creatinine (mg/dL)	1.0 ± 0.3	1.0 ± 0.3	1.0 ± 0.3	1.0 ± 0.3	0.067
eGFR	76.0 ± 34.1	106.1 ± 332.5	99.6 ± 134.3	85.5 ± 41.8	0.072
History of Hypertension	84 (61.8%)	72 (53.3%)	89 (66.4%)	64 (47.4%)	0.008
Hypercholesterolemia	79 (58.1%)	69 (51.1%)	76 (56.7%)	87 (64.4%)	0.174
History of Previous MI	27 (19.9%)	22 (16.3%)	16 (11.9%)	21 (15.6%)	0.364
Current Smoker	63 (46.3%)	51 (37.8%)	52 (38.8%)	51 (37.8%)	0.427

The analysis revealed that serum adiponectin level was a potent, graded, and independent predictor of the outcome. In both unadjusted and adjusted models, lower adiponectin quartiles were associated with a significantly higher risk in a dose-response manner. Compared to the highest quartile (Q4, reference), participants in the lowest quartile (Q1) had more than a four-fold higher unadjusted risk (HR 4.12, 95% CI 3.10–5.48), which remained a strong 3.56-fold increased risk after adjustment (95% CI 2.62–4.84, $p < 0.001$). Similarly, higher baseline HbA1c was an independent risk factor, with each percentage increase associated with a 32% higher adjusted risk (aHR 1.32,

95% CI 1.15–1.51, p < 0.001). Increased waist circumference also showed a small but statistically significant independent association (aHR 1.02 per cm, 95% CI 1.00–1.04, p=0.045). In contrast, the effects of triglycerides, CRP, and age were not statistically significant in the fully adjusted model. These results indicate that lower adiponectin levels and higher HbA1c are the strongest and most consistent independent predictors of the studied outcome.

Predictor Variable	Unadjusted HR (95% CI)	P-value	Adjusted HR (95% CI)*	P-value
Quartile 4 (Highest)	1.00 (Reference)	—	1.00 (Reference)	—
Quartile 3	1.68 (1.24–2.28)	0.001	1.52 (1.10–2.10)	0.012
Quartile 2	2.45 (1.82–3.31)	<0.001	2.14 (1.55–2.96)	<0.001
Quartile 1 (Lowest)	4.12 (3.10–5.48)	<0.001	3.56 (2.62–4.84)	<0.001
Baseline HbA1C (%)	1.45 (1.28–1.64)	<0.001	1.32 (1.15–1.51)	<0.001
Waist Circumference (cm)	1.04 (1.02–1.06)	<0.001	1.02 (1.00–1.04)	0.045
Triglycerides (mg/dL)	1.01 (1.00–1.02)	0.015	1.01 (1.00–1.01)	0.082
CRP (log-transformed)	1.12 (0.98–1.28)	0.104	1.05 (0.92–1.20)	0.45
Age (per year)	1.01 (0.99–1.03)	0.245	1.00 (0.98–1.02)	0.882

Discussion and Limitation

The study identified that circulating adiponectin is a powerful and independent predictor of new-onset Type 2 Diabetes Mellitus (T2DM) in STEMI survivors without prior diabetes. Our findings demonstrate a striking dose-response relationship: compared to patients in the highest adiponectin quartile, those in the lowest quartile faced a more than three-fold higher risk of developing T2DM (aHR 3.56) even after comprehensive adjustment for established metabolic risk factors, including HbA1c and waist circumference. This association underscores adiponectin's role beyond a mere biomarker, positioning it as a central player in the pathophysiology linking myocardial infarction to subsequent metabolic deterioration. The pronounced gradient of risk across quartiles aligns with research done by Li et al., which also found an inverse association between adiponectin and diabetes risk.(6)

The cohort consisted of middle-aged STEMI survivors characterized by a substantial burden of cardiometabolic risk factors, including elevated HbA1c, dyslipidemia, abdominal obesity, and systemic inflammation. This profile is consistent with the "metabolically unhealthy" phenotype often observed post-MI. The stratification by adiponectin quartiles (Table 2) revealed a coherent metabolic pattern. Lower adiponectin levels were strongly and significantly associated with a worse profile across nearly all modifiable risk metrics. Patients in the lowest adiponectin quartile exhibited significantly higher waist circumference, HbA1c, triglycerides, uric acid, and liver enzymes (ALT, GGT), alongside lower HDL cholesterol. This clustering of insulin resistance, visceral adiposity, and hepatic steatosis markers with hypoadiponectinemia corroborates the established biological functions of adiponectin in enhancing insulin sensitivity, promoting fatty acid oxidation, and exerting anti-inflammatory effects.(7–9) The lack of significant association with CRP in our models, despite elevated median levels, suggests that adiponectin's predictive power operates through pathways distinct from or additive to systemic inflammation measured by CRP in this context.

Our results reinforce and quantify the independent predictive value of two key parameters: adiponectin and HbA1c. While the association between higher baseline HbA1c (aHR 1.32 per %) and increased diabetes risk is expected and consistent with prediabetes pathophysiology, the magnitude and independence of the adiponectin association are particularly notable. The fact that the strength of adiponectin's association was only partially attenuated upon adjustment for HbA1c and waist circumference indicates it captures a unique dimension of risk—likely related to deeper adipose tissue dysfunction and its systemic metabolic effects. This finding is crucial for risk stratification,

suggesting that measuring adiponectin post-STEMI could identify a subset of patients at exceptionally high risk for T2DM who might benefit from intensive, targeted lifestyle or pharmacological interventions aimed at improving adipocyte function and insulin sensitivity. The study by von Eynatten et al. in patients with coronary artery disease similarly highlighted adiponectin as a predictor of cardiovascular events.(10)

The prospective design and 100% follow-up completion lend considerable credibility to our findings. However, certain limitations must be acknowledged. The single-center design may limit generalizability, and residual confounding from unmeasured factors like diet, physical activity, or genetic predisposition is possible. Furthermore, while we adjusted for key confounders, the observational nature precludes definitive causal inference. Future research should focus on interventional studies to determine whether strategies aimed at raising adiponectin levels (e.g., through thiazolidinediones, weight loss, or exercise) can effectively reduce the incidence of T2DM in this vulnerable post-STEMI population. In conclusion, low plasma adiponectin concentration is a strong and independent predictor of new-onset T2DM in non-diabetic STEMI patients, providing a valuable biomarker for identifying individuals who warrant aggressive preventive strategies to mitigate the dual burden of cardiovascular and metabolic disease.

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