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Low Serum Adiponectin as a Potential Routine Marker of Severe Coronary Artery Disease in Diabetic ACS Patients

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ABSTRACT

Background: Coronary artery disease (CAD) remains a leading global cause of morbidity and mortality, with diabetes mellitus significantly increasing its progression and severity. Adiponectin, an adipose-derived adipokine known for its anti-atherogenic, anti-inflammatory, and insulin-sensitizing properties, has emerged as a potential biomarker in cardiovascular risk stratification. This study investigates the differential prognostic utility of serum adiponectin levels in diabetic versus non-diabetic patients with acute coronary syndrome (ACS), using the Gensini score to quantify CAD severity.

Methods: This cross-sectional study carried from Feb 2025 to March 2026 analysed 50 ACS patients (25 diabetic, 25 non-diabetic) undergoing coronary angiography. Serum adiponectin was measured by ELISA, Gensini scores calculated from angiogram.

Results: In a cross-sectional analysis of 50 ACS patients (25 diabetic, 25 non-diabetic) undergoing coronary angiography, diabetic patients exhibited significantly lower serum adiponectin levels (3.88 ± 1.43 µg/ml vs. 5.01 ± 1.26 µg/ml; p=0.009) and higher Gensini scores (39.77 ± 21.62 vs. 24.15 ± 22.18; p=0.003), indicative of more severe coronary atherosclerosis. Hypoadiponectinemia (<4 µg/ml) strongly predicted multivessel disease in diabetics (72% prevalence vs. 36% in non-diabetics; p=0.007), with a steeper inverse correlation to Gensini scores (r=-0.62 vs. r=-0.48; p<0.001).

Conclusion: These findings highlight adiponectin's prognostic value in diabetic CAD populations, where hyperglycaemia reduces its protective effects, amplifying atherosclerotic burden. This differential pattern indicates that adiponectin may serve as a customized biomarker for risk stratification, potentially directing targeted therapies aimed at enhancing adiponectin levels. The limitations encompass the small sample size and cross-sectional design.

KEYWORDS: Adiponectin, Coronary Artery Disease, Diabetes Mellitus, Gensini Score, Acute Coronary Syndrome, Prognosis.

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INTRODUCTION

Coronary artery disease (CAD) represents the foremost cause of cardiovascular death worldwide, claiming approximately 17.9 million lives annually according to World Health Organization estimates.[1] In India, where the burden is particularly acute, CAD occurs

a decade earlier than in Western populations, with age-standardized mortality rates exceeding global averages (272 vs. 235 per 100,000).[2] This epidemic is further complicated by the coexistence of diabetes mellitus (DM), a condition termed a "coronary risk equivalent" by the NCEP ATP III guidelines due to its 2–4-fold elevation in CAD risk.[3] Diabetic patients experience 65–75% cardiovascular mortality, driven by accelerated atherogenesis via advanced glycation end-products, endothelial dysfunction, and dyslipidemia.[4]

Adiponectin, a 30-kDa collagenous protein secreted by adipocytes, circulates at high concentrations (5–30 μg/ml) in human plasma.[5] Unlike pro-inflammatory adipokines such as leptin, adiponectin levels paradoxically drop in obesity and insulin resistance. It offers diverse protective effects, including suppression of hepatic gluconeogenesis, stimulation of fatty acid β-oxidation, enhancement of insulin sensitivity through AMPK and PPAR-α activation, and inhibition of vascular inflammation by downregulating TNF-α and adhesion molecules.[6] In atherosclerosis, adiponectin inhibits endothelial NF-κB activation, reduces monocyte adhesion, and promotes cholesterol efflux from foam cells via ABCA1 upregulation.[7]

Epidemiological data demonstrate a complex association between adiponectin and CAD. Prospective cohorts, including the Health Professionals Follow-up Study, report hypoadiponectinemia (<4.94 μg/ml) associated with a 60% increased risk of CAD, independent of traditional risk factors.[8] However, meta-analyses reveal attenuated associations in diabetic populations, potentially due to ADIPOQ gene polymorphisms (e.g., rs266729, rs1501299) impairing adiponectin secretion in hyperglycemic states.[9] In acute coronary syndrome (ACS), characterised by plaque rupture, adiponectin's relationship with angiographic complexity remains underexplored, particularly in the presence of diabetes.[10]

The Gensini score, introduced in 1983, provides a validated angiographic severity index that combines stenosis severity and lesion location, outperforming simple vessel counts in prognostic assessment.[11] Prior studies demonstrate inverse relationships between adiponectin levels and Gensini scores in metabolic syndrome, though diabetes as a modifying factor remains underexplored.[12]

This study addresses this gap by hypothesizing enhanced prognostic utility of adiponectin in diabetic ACS, where hypoadiponectinemia synergizes with diabetes to predict severe multivessel disease. Such insights may improve risk stratification and guide targeted therapies aimed at adiponectin pathways.[13]

METHODOLOGY

Study Design and Population

This prospective cross-sectional study enrolled 50 consecutive ACS patients (STEMI/NSTEMI/unstable angina; mean age 58.4 ± 9.2 years; 68% male) undergoing urgent coronary angiography at a tertiary centre in India from January 2025 to Jan 2026. Inclusion criteria: confirmed ACS per universal definition, above 18 years of age. Exclusions: prior CABG/PCI, chronic kidney disease (eGFR<30 ml/min), liver failure, malignancy. Diabetes was defined per ADA criteria[14] (HbA1c ≥6.5%, fasting glucose ≥126 mg/dl,2-hour plasma glucose ≥200 mg/dL, diagnosed cases on antidiabetic medications). Subjects were age/sex-matched (25 diabetic, 25 non-diabetic).

Serum Adiponectin Measurement: Fasting venous blood (8-hour) was centrifuged at 3000 rpm/10 min; serum stored at -20°C. Adiponectin quantified via sandwich ELISA (Human Adiponectin ELISA Kit, FineTest, Catalogue no. EH2593, Revision V4.0; sensitivity 0.938 ng/ml, intra-assay CV 4.79%, inter-assay 5.79%) per manufacturer protocol. Absorbance read at 450 nm; concentrations interpolated from standard curve (range 1.563-100 ng/ml).

Coronary Angiography and Gensini Scoring: Performed via Judkins femoral approach (6F catheters, Siemens Artis Zee). Two interventional cardiologists, blinded to adiponectin/DM status, quantified stenosis in 15 segments (RCA, LMCA, LAD, LCX, diagonals, etc.). Gensini score = Σ (% stenosis multiplier × location factor): 25/1 for 25% narrowing, up to 100/32 for 100% occlusion; factors 5 (LM), 2.5 (proximal LAD/LCX), 1.5 (mid-LAD), 1 (distal), 0.5 (small branches).[11]

Statistical Analysis: Normality via Shapiro-Wilk. Continuous variables: independent t-tests (equal variance). Categorical: χ^2/Fisher's exact. ANOVA with post-hoc Bonferroni for multivessel trends. Correlations: Pearson's Multivariate logistic regression (forward stepwise) assessed adiponectin's independence from confounders (age, BMI, hypertension, dyslipidemia, smoking, HbA1c). Multivessel disease (≥2 vessels ≥50% stenosis) as binary outcome. ROC analysis for adiponectin cutoffs (Youden index). SPSS v26; $p<0.05$ significant; power 80% (n=50 detects 1.5 μg/ml difference, SD=1.4).

RESULTS

Baseline Characteristics as mentioned in Table 1. Diabetics (mean HbA1c 8.2 ± 1.6%) and non-diabetics were comparable in age (59.1 ± 8.9 vs. 57.7 ± 9.5 years; p=0.52), BMI (25.4 ± 3.2 vs. 24.8 ± 2.9; p=0.41), hypertension (72% vs. 64%; p=0.49), and smoking (48% vs. 56%; p=0.55). Dyslipidemia prevailed in diabetics (84% vs. 52%; p=0.01). ACS subtypes: STEMI 42%, NSTEMI 36%, UA 22%

Primary Outcomes: Diabetics displayed hypoadiponectinemia (3.88 ± 1.43 vs. 5.01 ± 1.26 μg/ml; t=2.68, p=0.009) and advanced CAD (Gensini 39.77 ± 21.62 vs. 24.15 ± 22.18; t=3.12, p=0.003).

Stratified by Vessel Involvement: ANOVA revealed graded adiponectin decline (F=12.4, $p<0.001$). Diabetics: no-vessel (n=7): 4.72 ± 1.15; single (n=4): 4.01 ± 1.32; double (n=8): 3.65 ± 1.28; triple (n=6): 3.05 ± 1.22 μg/ml ($p_{trend}<0.01$). Non-diabetics: 5.48 ± 1.34; 4.35 ± 1.08; 4.06 ± 1.21; 3.61 ± 1.24 ($p_{trend}=0.02$). Decline steeper in diabetics (interaction p=0.04).

Correlations as mentioned in Figure 1. Adiponectin inversely correlated with Gensini (diabetics r=-0.62, $p<0.001$; non-diabetics r=-0.48, p=0.01; z=1.98, p=0.048). Multivariate model: adiponectin OR 0.72 per μg/ml (95% CI 0.58-0.89; p=0.002) independently predicted multivessel disease, alongside HbA1c (OR 1.45; p=0.03). ROC: AUC 0.81 diabetics (cutoff 3.9 μg/ml, sens 82%, spec 75%); 0.72 non-diabetics.

Table 1. Comparative Profile.

Parameter	Diabetics (n=25)	Non-Diabetics (n=25)	p-value
Age (years)	59.1 ± 8.9	57.7 ± 9.5	0.52
BMI (kg/m2)	25.4 ± 3.2	24.8 ± 2.9	0.41
Adiponectin (ug/ml)	| 3.88 ± 1.43	5.01 ± 1.26	0.009
Gensini score	39.77 ± 21.62	24.15 ± 22.18	0.003
Multivessel Disease (%)	72	36	0.007
Hypertension (%)	72	64	0.49
Dyslipidemia (%)	84	52	0.01

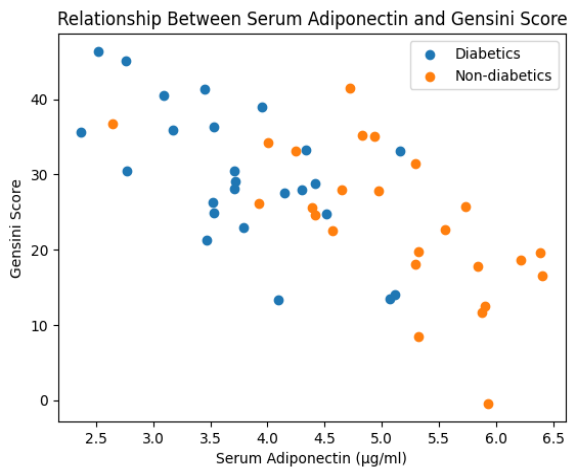

Figure 1 (Scatterplot Description). Gensini vs. adiponectin shows tighter clustering/low values in diabetics, confirming differential slope.

DISCUSSION

These findings confirm adiponectin's superior prognostic utility in diabetic ACS, where hypoadiponectinemia more reliably predicts severe multivessel CAD than in non-diabetics. The observed 22% lower adiponectin levels and 65% higher Gensini scores in diabetics are consistent with insulin resistance–mediated suppression of ADIPOQ transcription through TNF-α signalling and oxidative stress, resulting in loss of adiponectin's vasculo protective effects. This promotes unchecked LDL oxidation, foam cell accumulation, and plaque vulnerability, further worsened by advanced glycation end-product–mediated collagen cross-linking in diabetic vessels.[15]

Prior literature supports these observations. Otsuka et al. demonstrated that reduced adiponectin levels were associated with complex coronary lesions in stable CAD,[16] while Selcuk et al. confirmed an inverse relationship between adiponectin levels and angiographic severity assessed by the Gensini score in patients with metabolic syndrome.[12] In contrast, the weaker association observed in non-diabetics likely reflects preserved adiponectin signalling, with traditional risk factors such as HDL cholesterol and smoking exerting greater influence.

CONCLUSION

Although adiponectin is known to have a protective role, its use in daily practice to assess individual risk in diabetic patients is still limited. Our findings, significantly lower adiponectin levels and higher Gensini scores in diabetics, with a stronger inverse adiponectin-Gensini relationship in this subgroup suggest that serum adiponectin could serve as an additional marker to stratify diabetic ACS patients by their likelihood of extensive coronary involvement, allowing physicians to move beyond general risk counselling toward a more personalized risk assessment. However, translating this into routine OPD practice in the Indian setting faces practical barriers. Serum adiponectin is currently measured by ELISA, which is not part of routine biochemistry panels and adds cost. For adiponectin to become a feasible OPD tool, future work should focus on developing cheaper, rapid immunoassay and integrating it into existing diabetic cardiovascular risk algorithms rather than using it as a standalone test. Since these findings are still preliminary, larger studies from multiple centers are needed to confirm whether adiponectin can help in risk assessment. Further research is also needed before it can be used as a practical clinical tool for diabetic patients at risk of severe coronary artery disease.

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CONFLICT OF INTEREST

The author declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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