Section: Clinical Chemistry

Original Research Article

# A COMPARATIVE STUDY OF NOVEL INFLAMMATORY MARKERS - BETA-2 MICROGLOBULIN AND SERUM PROGRANULIN IN PATIENTS WITH ACUTE CORONARY SYNDROME: CORRELATION WITH LIPID PROFILE AND DISEASE SEVERITY

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## ABSTRACT

**Background:** Acute Coronary Syndrome (ACS), encompassing spectrum of unstable angina to myocardial infarction, remains a leading cause of global morbidity and mortality. The underlying pathogenesis is firmly rooted in atherosclerosis, a chronic inflammatory disease of the arterial wall. Commonly measured systemic inflammatory markers, like high-sensitivity C-reactive protein (hs-CRP), provide some prognostic information but lack specificity for the vascular inflammatory milieu. Novel, clinically relevant inflammatory biomarkers like serum Beta-2 microglobulin (B2M) and serum Progranulin (PGRN), offer a more integrative assessment of coronary artery disease (CAD) activity and severity. **Objectives:**To compare and evaluate the profile of novel and conventional inflammatory biomarkers in patients with Acute Coronary Syndrome (ACS) with matched controls and to assess their correlation with lipid indices and the angiographic severity of coronary artery disease.**Method:** Inflammation and dyslipidemia being the cornerstone of atherogenesis,we compared the novel inflammatory markers B2M and PGRN in patients diagnosed as ACS with non Myocardial Infarction (non MI) subjects. A hospital-based, analytical, case-control study was conducted in our tertiary care centre. Acute Myocardial infarction cases, (n=22) Age- and sex-matched individuals with a negative cardiac troponin T test served as Control Group(n=22). Creatine Kinase-MB (CK-MB), Lactate Dehydrogenase (LDH), Lipid Profile, Angiographic data including number of vessels involved and severity of stenosis were considered. B2M and PGRN were measured in both groups and correlated with lipid parameters, conventional markers of MI, angiographic severity of coronary vessel occlusion. Spearman's rank correlation was used and statistical analysis made using SPSS software. (version 25). **Results:** Beta-2 Microglobulin (B2M) levels were markedly higher in ACS patients (Median: 2.10 mg/L, IQR: 1.50-11.03) versus controls (Median: 1.30 mg/L, IQR: 1.20-1.40; $p<0.001$). Similarly, Progranulin (PGRN) levels were significantly elevated in the ACS group (Median: 0.46 ng/mL, IQR: 0.32-0.66) compared to the control group (Median: 0.13 ng/mL, IQR: 0.11-0.15; $p<0.001$). There were no significant differences in the lipid profile parameters between the two groups ($p>0.05$) except HDL ($p<0.0001$). The novel inflammatory markers B2M and PGRN were significantly elevated in MI and demonstrated strong, statistically significant correlations with objective measures of coronary disease severity as measured by the total occlusion score ($\rho = 0.723$, $p<0.001$, $\rho = 0.584$, $p<0.01$) respectively. **Conclusion:** B2M and PGRN are promising novel and dynamic markers reflecting the acute inflammatory surge in ACS and the extent of coronary vessel occlusion.

## INTRODUCTION

Acute Coronary Syndrome (ACS), encompassing spectrum of unstable angina to myocardial infarction, remains a leading cause of global morbidity and mortality.[1] The underlying pathogenesis is firmly rooted in atherosclerosis, a chronic inflammatory disease of the arterial wall.[2] Inflammation is not merely a background process but plays a central role in plaque initiation, progression, and the transition to a vulnerable state prone to rupture and thrombosis.[3] In clinical practice, the diagnosis and risk stratification of ACS rely on a combination of clinical presentation, electrocardiographic findings, and cardiac-specific biomarkers such as cardiac Troponins (cTn) and Creatine Kinase-MB (CK-MB).[4] For myocardial ischemia or necrosis, they offer limited insight into the ongoing inflammatory activity that predisposes to the event. Systemic inflammatory markers, like high-sensitivity C-reactive protein (hs-CRP), provide prognostic information but lack specificity for the vascular inflammatory milieu.[5]

This gap underscores the need for novel, pathophysiologically relevant inflammatory biomarkers that can be reliable for integrative assessment of coronary artery disease (CAD) activity based on extent of inflammation and severity. Two such promising candidates are serum Beta-2 microglobulin (B2M) and serum Progranulin (PGRN). B2M, a component of the major histocompatibility complex class I molecule, has emerged as a marker of inflammatory burden and cellular turnover, with elevated levels linked to adverse cardiovascular outcomes.[6] PGRN, a multifunctional glycoprotein with potent anti-inflammatory properties, plays a complex role in tissue repair, inflammation, and metabolic regulation.[7] Its precise role in the setting of acute coronary ischemia warrants further investigation.

The interplay between inflammation and dyslipidemia is a cornerstone of atherogenesis.[8] While the relationships between traditional lipid indices—low-density lipoprotein cholesterol (LDL-C), triglycerides, high-density lipoprotein cholesterol (HDL-C), and total cholesterol—and cardiovascular risk are well-established, their dynamic correlation with specific inflammatory pathways in ACS is less clearly defined. An integrated analysis linking novel inflammatory markers with both lipid profiles and the anatomical burden of the disease could provide a more holistic view of patient risk and severity of CAD.

Angiography provides the definitive anatomical assessment of CAD severity, including the number of diseased vessels and the degree of luminal obstruction.[9] Correlating biomarker levels with this gold-standard imaging may validate their role as indirect reflectors of coronary plaque burden and complexity. The search for biomarkers that extend beyond myocardial necrosis to reflect the inflammatory substrate of Acute Coronary Syndrome (ACS) is a dynamic area of cardiovascular research.

**Beta-2 Microglobulin in Cardiovascular Disease:**

Beta-2 microglobulin, a component of the major histocompatibility complex class I molecule, filtered and eliminated by the kidneys. B2M, a immunoglobulin light chain like peptide with molecular weight 11,800 Daltons, has a prominent Beta Pleated structure. Synthesis of B2M is stimulated by activation of complements and cytokine production. Beyond its renal association, it has been recognized as a marker of heightened cellular activity and inflammation. Elevated serum B2M has been independently associated with the presence and severity of atherosclerosis. A prospective cohort study by Liu et al. (2020) demonstrated that elevated B2M levels were a significant predictor of major adverse cardiovascular events (MACE) in patients with stable coronary artery disease, even after adjustment for traditional risk factors and renal function [10]. Its proposed mechanisms in atherogenesis include direct stimulation of inflammatory pathways within the vascular wall and promotion of vascular calcification.[11]

Insight to atherosclerotic changes-Inflammatory role of B2M is shown in Figure1.

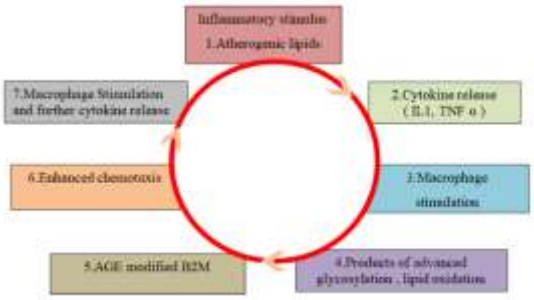


**Figure 1. Proposed role of B2M in Inflammation in CAD**

The reference interval of serum B2M is 0.7-1.8 mg /L.Urinary excretion is more than 300 mg/L. CSF 0-2.5 mg/L

**Progranulin: A Multifunctional Inflammatory Modulator**

Progranulin is a secreted, 80kDa cysteine rich glycoprotein, consisting of 7.5 tandem repeats termed as granulins. PGRN plays context-dependent roles in inflammation, tissue repair, wound healing, and cellular proliferation. It exerts potent anti-inflammatory effects by suppressing tumor necrosis factor-alpha (TNF-α) signaling mediated by IL-8.[12] Paradoxically, in chronic inflammatory states and during tissue repair GRN gene is upregulated and PGRN levels are elevated. Enzymatic cleavage by various proteases forming Granulins which is proinflammatory,[7] occurs at the site of damage and leads to inflammation. In cardiovascular disease, the data are emerging. Egashira et al. (2019) reported that higher serum PGRN levels were associated with the


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presence of coronary artery disease and were correlated with hs-CRP, indicating a link to systemic inflammation.[13] Furthermore, experimental models suggest PGRN may have a protective role in endothelial function and against atherosclerotic plaque progression.[14] The precise behavior and prognostic value of PGRN in the specific setting of ACS, particularly in relation to infarct size and coronary lesion complexity, require further elucidation.

**The Inflammation-Lipid Axis in Atherosclerosis:** The bidirectional relationship between dyslipidemia and inflammation is a fundamental pillar in understanding ACS. Atherogenic lipoproteins, particularly oxidized LDL, are not merely passive deposits but active participants in endothelial dysfunction and plaque inflammation, stimulating the release of cytokines and chemokines.[8,15] Conversely, inflammatory cytokines can alter lipid metabolism, reducing HDL functionality and increasing hepatic VLDL secretion.[16] While the individual roles of LDL, HDL, and triglycerides are well-characterized, studying their correlation with specific upstream inflammatory mediators like B2M and PGRN may reveal nuanced pathways linking metabolic risk to clinical events.

**Biomarkers and Angiographic Correlation**

Coronary angiography is the gold standard for defining the anatomic extent and severity of CAD. Correlating serum biomarker levels with angiographic findings strengthens their validity as indicators of disease burden. Studies have established links between hs-CRP and complex lesion morphology or multi-vessel disease.[17] Similarly, lipoprotein(a) and apolipoprotein B have shown correlations with coronary stenosis severity.[18] Investigating whether novel inflammatory markers like B2M and PGRN correlate with quantitative angiographic metrics—such as the Gensini score, SYNTAX score, or total occlusion burden—is a critical step in establishing their clinical relevance beyond circulating levels alone. A recent study by Chen et al. (2022) found that B2M levels were positively correlated with the SYNTAX score in patients with non-ST-elevation ACS, suggesting a link to angiographic complexity.[19] Research specifically linking B2M levels to the acute phase of myocardial infarction and to detailed angiographic findings, however, remains comparatively limited.

There is a paucity of studies that concurrently evaluate both B2M and PGRN in an ACS population. To perform a tripartite analysis, we aimed at: (1) comparing B2M and PGRN levels in ACS to healthy controls, (2) correlating them with a comprehensive lipid profile,markers of MI and (3) systematically associating them with angiographic severity scores and to determine whether novel markers B2M and PGRN provide complementary or independent information about the inflammatory-atherosclerotic process. The present study was conducted to integratively analyse these inflammatory biomarkers, traditional lipid indices, and coronary vascular pathology in ACS.

## MATERIALS AND METHODS

**Study Design:** A hospital-based, analytical, case-control study was conducted in the Department of Cardiology and the Cardiac Catheterization Laboratory and central diagnostic laboratory at Tirunelveli Medical College and Hospital. The data collection period spanned 12 months, from August 2024 to July2025. The study comprised two groups: Patients admitted with a confirmed diagnosis of Acute Myocardial Infarction (AMI), based on the Fourth Universal Definition of Myocardial Infarction (clinical symptoms, ECG changes, and elevated cardiac troponin T) were the cases. Age and sex-matched individuals with no clinical history or symptoms of coronary artery disease, presenting for routine health check-ups, and with a negative cardiac troponin T test served as control group.

**Sample Size:** The sample size was calculated using the formula for comparing two means. The primary outcome variable was serum Beta-2 Microglobulin (B2M) level. Based on previous literature and preliminary pilot data from our institution, the expected mean (±SD) B2M level was 4.5 ± 5.0 mg/L in the MI group and 1.3 ± 0.2 mg/L in the control group. With a 95% confidence level,the minimum required sample size was 24 participants per group (total N=48) was set.

Consecutive sampling was employed. All eligible patients admitted with AMI during the study period who met the inclusion criteria were invited to participate. Convenience sampling with frequency matching for age (±5 years) and sex was used to recruit controls from the outpatient department during the same period. Individuals with acute infections, auto immune disorders, Chronic kidney disease and malignancy were excluded from the study.

Demographic and clinical Data were collected and 5 ml of venous blood was drawn from each participant at admission (cases- MI) or during health check-up (Non MI -controls). Serum was analyzed for novel Inflammatory Markers, Beta-2 Microglobulin (B2M, mg/L) by nephelometry and Progranulin (PGRN, ng/mL from pilot study) using ELISA.

Conventional Cardiac & Inflammatory Markers: Cardiac Troponin T (cTnT, qualitative), Creatine Kinase-MB (CK-MB, U/L), Lactate Dehydrogenase (LDH, U/L) by spectrophotometry.

**Lipid Profile:** Low-Density Lipoprotein (LDL, mg/dL) calculated, Triglycerides (TGL, mg/dL), High-Density Lipoprotein (HDL, mg/dL), Total Cholesterol (mg/dL). measured by photometry.

**Angiographic Data (Case Group only):** Coronary angiography findings were recorded, including the number of significantly diseased vessels (≥70% stenosis) and the percentage of luminal obstruction in major coronary arteries (Left Anterior Descending LAD, Right Circumflex Artery RCA, Left


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Circumflex Artery LCA). A "Total Occlusion Score" was derived as the sum of the highest blockage percentages from the three major territories.

**Statistical Analysis:** Data were analyzed using IBM SPSS Statistics for Windows, Version 25.0. For demographic and comparative analysis appropriate statistical methods were used.

**Correlation Analysis:** Spearman's rank correlation coefficient (ρ) was used to assess the strength and direction of associations between novel markers (B2M, PGRN) and: (a) lipid parameters, and (b) markers of severity (CK-MB, Total Occlusion Score).

**Inferential Statistics:** A p-value of $< 0.05$ was considered statistically significant for all tests.

**Ethical Considerations:** The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and approved by the Institute Ethics Committee (IEC) of Tirunelveli Medical college.Written informed consent was obtained from all participants (or their legally authorized representatives in emergency cases) after explaining the study's nature, purpose, procedures, potential risks, and benefits. Participation was entirely voluntary.

Confidentiality was maintained in all aspects.

## RESULTS

A total of 44 participants were included in the final analysis: 22 patients in the Myocardial Infarction (MI) group and 22 matched individuals in the Non-MI control group. All statistical assumptions were tested prior to analysis.

**Baseline Demographic and Clinical Characteristics:** The baseline characteristics of both study groups are presented in [Table 1]. The study groups were well-matched for age and sex distribution, with no statistically significant differences ($p>0.05$), confirming the effectiveness of the matching protocol. As per the inclusion criteria, all patients in the MI group had a positive qualitative cardiac troponin T test, while all controls were negative.

**Table 1: Baseline Characteristics of Study Participants**

| Variables | MI Group (n = 22) | Non-MI Group (n = 22) | p-value |
|---|---|---|---|
| Age (years), Mean ± SD | 51.9 ± 10.5 | 46.8 ± 5.9 | 0.054† |
| Sex, n (%) | | | 0.763‡ |
| Male | 13 (59.1%) | 12 (54.5%) | |
| Female | 9 (40.9%) | 10 (45.5%) | |
| cTnT, n (%) | | | < 0.001‡ |
| Positive | 22 (100%) | 0 (0%) | |
| Negative | 0 (0%) | 22 (100%) | |
| Treatment, n (%) | | | N/A |
| Angioplasty | 17 (77.3%) | 0 | |
| CABG | 5 (22.7%) | 0 | |

†Independent Samples t-test; ‡Chi-square test

**Table 2: Comparison of Biochemical Markers between MI and Non-MI Groups**

| Marker | MI Group (n = 22) | Non-MI Group (n = 22) | p-value |
|---|---|---|---|
| CK-MB (U/L), Median (IQR) | 70.2 (16.0–102.0) | 13.8 (12.2–15.0) | < 0.001 |
| LDH (U/L), Median (IQR) | 362.0 (322.0–457.0) | 188.5 (183.0–192.0) | < 0.001 |
| β2-Microglobulin (mg/L), Median (IQR) | 2.10 (1.50–11.03) | 1.30 (1.20–1.40) | < 0.001 |
| Progranulin (ng/mL), Median (IQR) | 0.46 (0.32–0.66) | 0.13 (0.11–0.15) | < 0.001 |
| LDL (mg/dL), Mean ± SD | 92.2 ± 44.0 | 110.4 ± 10.7 | 0.076† |
| HDL (mg/dL), Mean ± SD | 34.9 ± 6.6 | 53.6 ± 5.2 | 0.0001† |
| Triglycerides (mg/dL), Mean ± SD | 114.2 ± 37.2 | 96.7 ± 10.8 | 0.089† |
| Total Cholesterol (mg/dL), Mean ± SD | 150.6 ± 44.1 | 180.1 ± 9.1 | 0.102† |

Mann-Whitney U Test; †Independent Samples t-test; IQR = Interquartile Range

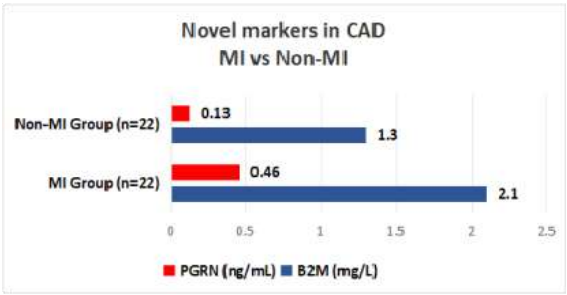


**Figure 2: Novel inflammatory markers in CAD - MI vs Non MI**

**Comparison of Biochemical Markers Between Groups:** The distribution of all biochemical markers was assessed using the Shapiro-Wilk test. Lipid parameters (LDL, HDL, TGL, Total Cholesterol) were normally distributed, while cardiac and inflammatory markers (CK-MB, LDH, B2M, PGRN) were non-normally distributed. Therefore, group comparisons for the latter were performed using the Mann-Whitney U test [Table 2].

Serum levels of the conventional cardiac markers, CK-MB and LDH, were significantly elevated in the MI group compared to controls ($p<0.001$ for both). More notably, the novel inflammatory markers also showed highly significant differences. Beta-2 Microglobulin (B2M) levels were markedly higher in MI patients (Median: 2.10 mg/L, IQR: 1.50-11.03) versus controls (Median: 1.30 mg/L, IQR: 1.20-1.40;


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p<0.001). Similarly, Progranulin (PGRN) levels were significantly elevated in the MI group (Median: 0.46 ng/mL, IQR: 0.32-0.66) compared to the control group (Median: 0.13 ng/mL, IQR: 0.11-0.15; p<0.001). There were no significant differences in the lipid profile parameters (LDL,TGL,Total Cholesterol) between the two groups (p>0.05) except for HDL(p<0.0001).

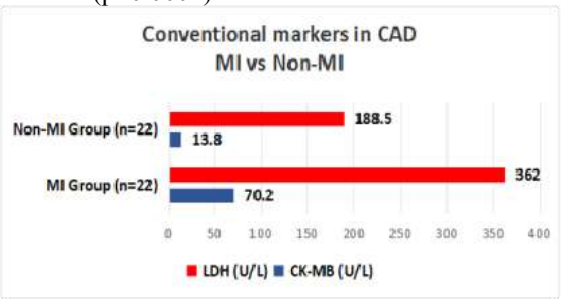


**Figure 3: Conventional markers MI and Non MI group**

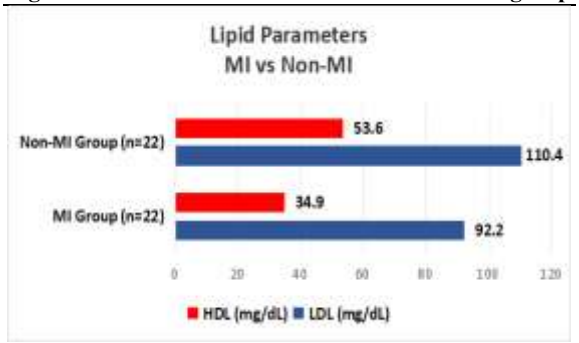


**Figure 4: Lipid parameters in MI and non MI group**

**Correlation Analysis in the MI Group:** Spearman's rank correlation (ρ) was used to assess relationship within the MI group.

**Correlation of Novel Markers with Lipids:** B2M showed a significant positive correlation with Total Cholesterol (ρ = 0.482, p=0.023) and a strong positive correlation with LDL (ρ = 0.681, p<0.001). It also correlated positively with TGL (ρ = 0.447, p=0.038) and negatively with HDL, though the latter was not significant (ρ = -0.378, p=0.084). PGRN demonstrated a moderate positive correlation with Total Cholesterol (ρ = 0.536, p=0.010) and LDL (ρ = 0.491, p=0.020).

**Correlation of Novel Markers with Disease Severity Indicators:** Both novel markers showed significant correlations with markers of myocardial injury and coronary disease burden. B2M correlated strongly with CK-MB (ρ = 0.610, p=0.003) and the angiographic Total Occlusion Score (ρ = 0.723, p<0.001). PGRN also showed significant, though slightly weaker, correlations with CK-MB (ρ = 0.487, p=0.021) and the Total Occlusion Score (ρ = 0.534, p=0.010). Furthermore, both B2M (ρ = 0.598, p=0.003) and PGRN (ρ = 0.452, p=0.036) were positively correlated with the number of significantly diseased coronary vessels.

**Table 3: Spearman's Correlation (ρ) of Novel Markers with Biochemical and clinical Parameters in the MI Group (n=22)**

| Parameter | B2M (mg/L) | | PGRN (ng/mL) | |
|---|---|---|---|---|
| | ρ | p-value | ρ | p-value |
| Lipid Profile | | | | |
| LDL (mg/dL) | 0.681 | < 0.001 | 0.491 | 0.02 |
| HDL (mg/dL) | −0.378 | 0.084 | −0.212 | 0.347 |
| TGL (mg/dL) | 0.447 | 0.038 | 0.301 | 0.174 |
| Total Cholesterol (mg/dL) | 0.482 | 0.023 | 0.536 | 0.01 |
| Severity Indicators | | | | |
| CK-MB (IU/L) | 0.610 | 0.003 | 0.487 | 0.021 |
| Total Occlusion Score (%) | 0.723 | < 0.001 | 0.534 | 0.01 |
| Number of Diseased Vessels | 0.598 | 0.003 | 0.452 | 0.036 |

In summary, the novel inflammatory markers B2M and PGRN were significantly elevated in MI patients and demonstrated strong, statistically significant correlations with key atherogenic lipids (LDL, Total Cholesterol) and, most notably, with objective measures of coronary disease severity and myocardial injury.

## DISCUSSION

A comparative study of inflammatory biomarkers in Acute Coronary Syndrome, with a focused investigation into the relationship between novel markers, lipid metabolism, and coronary anatomical severity was performed. The principal findings confirmed our hypotheses: serum levels of both Beta-2 Microglobulin (B2M) and Progranulin (PGRN) were significantly elevated in patients with MI compared to matched controls. These novel markers exhibit significant correlations with key atherogenic lipid components and with angiographic and functional indices of disease severity.

The marked elevation of B2M in the MI cohort aligns with evidences implicating it in cardiovascular pathogenesis.[11] B2M is not merely a renal function surrogate; it is actively involved in inflammatory pathways, including the stimulation of monocyte activation and endothelial inflammation.[20] Our findings corroborate previous studies that identified elevated B2M as an independent predictor of adverse cardiovascular events and severity in stable CAD and heart failure populations.[10,21] The novel contribution of this study was the demonstration of its acute-phase elevation in confirmed MI and its strong, graded correlation with the anatomical burden of disease as


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measured by the total occlusion score ($\rho = 0.723$, $p<0.001$) and number of diseased vessels. This suggests B2M may be a dynamic marker, reflecting not just chronic inflammatory burden but also the acute inflammatory surge associated with plaque rupture and its link to the extent of coronary atherosclerosis.

Similarly, the significant rise in PGRN levels in MI cases added a nuanced layer to the understanding of this multifunctional protein in ACS. While PGRN was known for its anti-inflammatory and tissue reparative actions in experimental models,[12] its elevated serum levels in chronic inflammatory diseases were thought to represent a counter-regulatory response.[7] Our results support the latter context in ACS. The elevated PGRN likely signifies a systemic attempt to modulate the intense post-infarct inflammatory response. This finding is consistent with recent clinical data showing higher PGRN levels in patients with CAD.[13] The significant correlation of PGRN with the total occlusion score indicates that the magnitude of this compensatory anti-inflammatory response is proportional to the anatomical severity of the ischemic insult.

A key objective of this study was to examine the interplay between inflammation and dyslipidemia. The lack of a significant difference in traditional lipid parameters (LDL, Total cholesterol, TGL) between the MI and control groups was unexpected but may be attributed to the acute-phase response of MI, which can transiently alter lipid levels, and the widespread use of statins. However, within the MI group, the correlation analysis revealed insightful relationships. The strong positive correlation between B2M and LDL ($\rho = 0.681$) and Total Cholesterol underscores a potential patho physiological link. Atherogenic LDL particles, particularly when oxidized, are potent inducers of vascular inflammation.[15] B2M, in turn, may exacerbate this process, creating a vicious cycle that promotes plaque instability. This correlation suggests that B2M might serve as an integrative marker linking dyslipidemia to its inflammatory consequences within the coronary vasculature.

The most clinically relevant findings are the robust correlations between both novel biomarkers and objective measures of disease severity. The strong association with CK-MB confirms their link to the magnitude of myocardial necrosis. The positive correlations with the angiographic total occlusion score and the number of diseased vessels provide compelling evidence that B2M and PGRN levels reflect the anatomical extent and complexity of coronary atherosclerosis. This aligns with emerging data; for instance, Chen et al. (2022) similarly found B2M levels correlated with the SYNTAX score in Non STEMI-ACS patients.[19] These correlations suggest that measuring B2M, PGRN in serum could offer a non invasive evidence as indicator of severity of coronary artery disease burden, potentially prove useful in risk stratification.

**Study Limitations:** Several limitations must be acknowledged. First, the single-center design and modest sample size may limit the generalizability of the findings. Second, the cross-sectional nature of the study establishes association but cannot infer causality or define the temporal relationship between biomarker elevation and the acute event. Third, while we controlled for age and sex, we did not adjust for all potential confounders such as renal function (e.g., eGFR), which can affect B2M levels, or other comorbidities. Fourth, PGRN was measured as a total serum level; its biological activity and cleavage into granulins, which have opposing functions, were not assessed.

## CONCLUSION

This study concluded that the novel inflammatory biomarkers Beta-2 Microglobulin and Progranulin were significantly elevated in Acute Coronary Syndrome. Their strong correlation with the angiographic severity of coronary atherosclerosis prove their potential role as integrative biomarkers that reflect the underlying inflammatory activity linked to plaque burden. Conventional troponins remain the cornerstone for diagnosing myocardial necrosis, B2M and PGRN may provide complementary information regarding the inflammatory activity and extent of coronary disease. These findings underscore the importance of the inflammation-lipid-axis in atherosclerosis and highlight promising candidates for enhancing risk stratification in CAD.

## REFERENCES


1. World Health Organization. Cardiovascular diseases (CVDs) [Internet]. 2021 [cited 2023 Oct 10]. Available from: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)
2. Ross R. Atherosclerosis—an inflammatory disease. N Engl J Med. 1999 Jan 14;340(2):115-26.
3. Libby P, Buring JE, Badimon L, Hansson GK, Deanfield J, Bittencourt MS, et al. Atherosclerosis. Nat Rev Dis Primers. 2019 Aug 16;5:56.
4. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth universal definition of myocardial infarction (2018). Eur Heart J. 2019 Jan 14;40(3):237-69.
5. Ridker PM. A test in context: high-sensitivity C-reactive protein. J Am Coll Cardiol. 2016 Feb 16;67(6):712-23.
6. Fanchao Shi,Luanluan Sun, Stephen Kaptoge, Association of beta-2-microglobulin and cardiovascular events and mortality: A systematic review and meta-analysis.Atherosclerosis.Volume 320, March 2021, Pages 70-78
7. Lucie Andrés Cerezo 1, Markéta Kuklová 1, Hana Hulejová 1, Zdeňka Vernerová 2, Nikola Kaspříková 3, et al.Progranulin Is Associated with Disease Activity in Patients with Rheumatoid Arthritis.Mediators Inflamm. 2015 Aug 3;2015:740357. doi: 10.1155/2015/740357
8. Tall AR, Yvan-Charvet L. Cholesterol, inflammation and innate immunity. Nat Rev Immunol. 2015 Feb;15(2):104-16.
9. Scanlon PJ, Faxon DP, Audet AM, Carabello B, Dehmer GJ, Eagle KA, et al. ACC/AHA guidelines for coronary angiography: executive summary and recommendations. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on




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Coronary Angiography). Circulation. 1999 May 4;99(17):2345-57.
10. Hang Fang 1, Qiankun Zhang 2, Lie Jin 2, 3,Association of beta-2-microglobulin with cardiovascular and all-cause mortality in the general and non-CKD population.Medicine (Baltimore) 2023 Mar 17;102(11):e33202. doi: 10.1097/MD.0000000000033202.
11. Jasmin Amighi 1, Matthias Hoke, Wolfgang Mlekusch, Oliver Schlager, Markus Exner, Markus Haumer, etal.Beta 2 microglobulin and the risk for cardiovascular events in patients with asymptomatic carotid atherosclerosis .Stroke. 2011 Jul;42(7):1826-33.
12. Yoji Kojima a, Koh Ono a, Katsumi Inoue b, Yasushi Takagi c, Ken-ichiro Kikuta c, Masaki Nishimura c,et al. Progranulin expression in advanced human atherosclerotic plaque.Atherosclerosis.Volume 206, Issue 1, September 2009, Pages 102-108
13. Ali Saeedi Boroujeni1 , Daryush Purrahman2 , Ali Shojaeian3 Fatemeh Rafiee5 , Łukasz A. Poniatowski4 , and Mohammad Reza Mahmoudian Sani2,6*, Progranulin (PGRN) as a regulator of inflammation and a critical factor in the immunopathogenesis of cardiovascular diseases.JJournal of Inflammation https://doi.org/10.1186/s12950 023 00327 0
14. Wei J, Zhang L, Ding Y, Liu R, Guo Y, Hettinghouse A, Buza J, De La Croix J, et al. Progranulin promotes diabetic fracture healing in mice with type 1 diabetes. Ann Transl Med. 2020 Mar;8(6):321.
15. Boren J, Chapman MJ, Krauss RM, Packard CJ, Bentzon JF, Binder CJ, et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease: pathophysiological, genetic, and therapeutic insights: a consensus statement from the European Atherosclerosis Society Consensus Panel. Eur Heart J. 2020 Jun 21;41(24):2313-30.
16. Feingold KR, Grunfeld C. The role of HDL in innate immunity. J Lipid Res. 2011 Jan;52(1):1-3.
17. Zouridakis E, Avanzas P, Arroyo-Espliguero R, Fredericks S, Kaski JC. Markers of inflammation and rapid coronary artery disease progression in patients with stable angina pectoris. Circulation. 2004 Oct 26;110(17):2607-11.
18. Tsimikas S, Fazio S, Ferdinand KC, Ginsberg HN, Koschinsky ML, Marcovina SM, et al. NHLBI Working Group Recommendations to Reduce Lipoprotein(a)-Mediated Risk of Cardiovascular Disease and Aortic Stenosis. J Am Coll Cardiol. 2018 Jan 16;71(2):177-92.
19. Chen X, Lin Y, Lin Z, Huang J. Serum β2-microglobulin levels are correlated with the severity of coronary artery disease and SYNTAX score in patients with NSTE-ACS. Cardiol Res Pract. 2022 May 31;2022:4790422.
20. Li Z, Jiao K, Chen M, Wang C, Wu D, Li M, et al. Beta-2-microglobulin exacerbates endotoxin-induced inflammatory response via promoting neutrophil infiltration and adhesion. Int Immunopharmacol. 2020 Jul;84:106520.
21. Song JW, Choi YJ, Lee S, Kim HJ, Lee MJ, Sim YJ, et al. Serum Beta-2 microglobulin level is an independent predictor of overall survival in patients with heart failure. Korean Circ J. 2020 Jun;50(6):532-44.


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