http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v11i5.01

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

# A Study to Measure Anti-Beta2 Glycoprotein1 Antibody Levels and to Assess their Association with the type of Acute Coronary Syndrome

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**Abstract**

**Background**: *Beta2 glycoprotein phospholipid cofactor is a natural anticoagulant and may act as an associated factor for acute myocardial infarction. Beta2 glycoprotein1 antibody has procoagulant tendency either in presence or absence of antiphospholipid syndrome.*

**Aim:** *The purpose of this study was to measure anti-beta2glycoprotein1 IgA (AB2GP1 IgA) antibody levels and to assess the association it has with the type of Acute Coronary Syndrome (ACS).*

**Methods**: *A hospital-based cross-sectional research was conducted on individuals with ACS who were above the age of 18.*

**Results:** *Among 30 patients of Acute coronary syndrome (ACS), 8 (26.7%) were NSTEMI, 12 (40%) were STEMI and 10 (33.3%) were Unstable Angina patients. More than half (53%) of all the 30 ACS patients had normal levels of AB2GP1 IgA antibody. More than half (58.3%) of the STEMI patients had high levels of AB2GP1 IgA antibody. About 25% of NSTEMI and 50% of unstable angina patients had high levels of AB2GP1 IgA antibody. Half of the male patients and 52.9% of those less than 50 years had high levels of AB2GP1 IgA antibody. Among co-morbidities and other risk factors 53.3% of T2DM and 38.5% of SHTN patients, 50% and 55.6% of those with alcohol consumption and smoking respectively were having high levels of AB2GP1 IgA antibody. But as the study was involving a small sample size none of these associations were found to be statistically significant ($p>0.05$).*

**Conclusion:** *IgA anti-beta2 glycoprotein 1 antibodies may be one of the possible markers for the onset and outcome of ACS, as it may be involved in the thrombotic events underlying ACS and could be an independent risk factor for MI in the general population. But further studies with a larger sample size and using probability sampling methodsare needed to determine its role and marker status in ACS.*

## Introduction

Acute coronary syndrome (ACS), according to the recently accepted classification, is a composition of three classical syndromes: unstable angina (UA), myocardial infarction (MI) without ST elevation (NSTEMI) or MI with ST elevation on ECG (STEMI). Thus NSTEMI and STEMI are forms of MI with troponin positivity, while UNSTABLE ANGINA is associated with negative troponin test[1]. The beta2-glycoprotein 1 phospholipid cofactor is a natural anticoagulant[2]. Antiphospholipid antibodies characterize patients at risk for both arterial and venous thrombotic events[4]. Antiphospholipid antibodies especially anti-beta2 glycoprotein 1 antibodies, may be involved in the current events undergoing in ACS[1]. IgA anti- beta2 glycoprotein 1 antibodies may be the most relevant for the onset and outcome of ACS[1]. Beta 2 glycoprotein 1 has been proposed to be involved in a range of physiological processes including clot formation, fibrinolysis, cell activation, immune responses, apoptosis, angiogenesis, coagulation and complement[6].

Beta 2 glycoprotein phospholipid cofactor is a natural anticoagulant and act as independent risk factor for acute myocardial infarction[2].Beta 2 glycoprotein 1, a ubiquitous phospholipid-binding plasma protein, is the main antigenic target for antiphospholipid antibodies relevant in antibody-mediated atherothrombotic diseases[9].

## Aims and Objectives

1. To measure anti-beta2 glycoprotein 1 IgA antibody levels in patients with Acute Coronary Syndrome.
2. To find the association of anti-beta2 glycoprotein 1 IgA antibody levels with the type of Acute Coronary Syndrome.

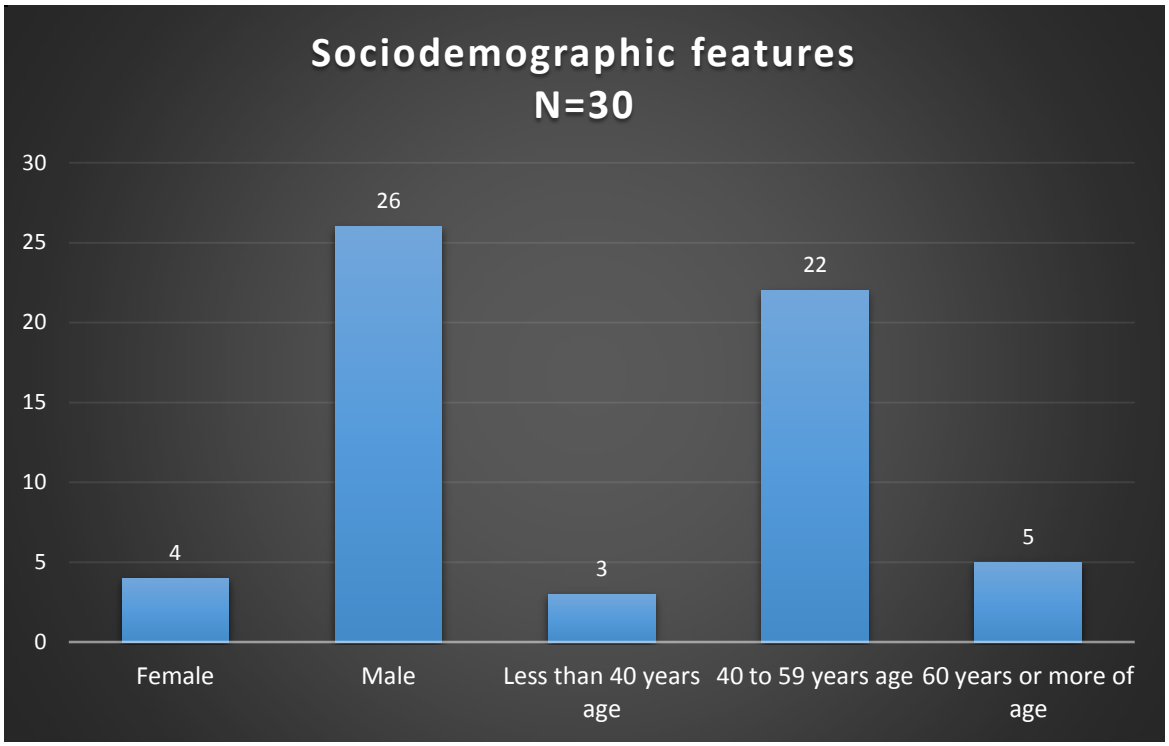
## Materials and Methods

A hospital-based cross-sectional research was conducted on individuals with ACS who were above the age of 18 years. A total of 30 people were included in the study using purposive sampling method. Cardiovascular risk factors, such as dyslipidemia, obesity, smoking, hypertension, diabetes, as well as previous cardiovascular, cerebrovascular and thrombotic events were determined according to the medical history and present clinical symptoms were assessed by history and clinical examination. Patients were categorized into three groups based on the three classes of ACS (STEMI/NSTEMI/ UNSTABLE ANGINA) depending on their ECG changes, Cardiac Enzyme levels and ECHO findings. The presence of antiphospholipid antibodies anti beta2 glycoprotein 1 IgA were determined in blood samples taken immediately after hospitalization by ELISA method in all these patients. The results obtained from these study group were assessed to find the association of antiphospholipid antibodies anti-beta2 glycoprotein IgA in patients with type of ACS.

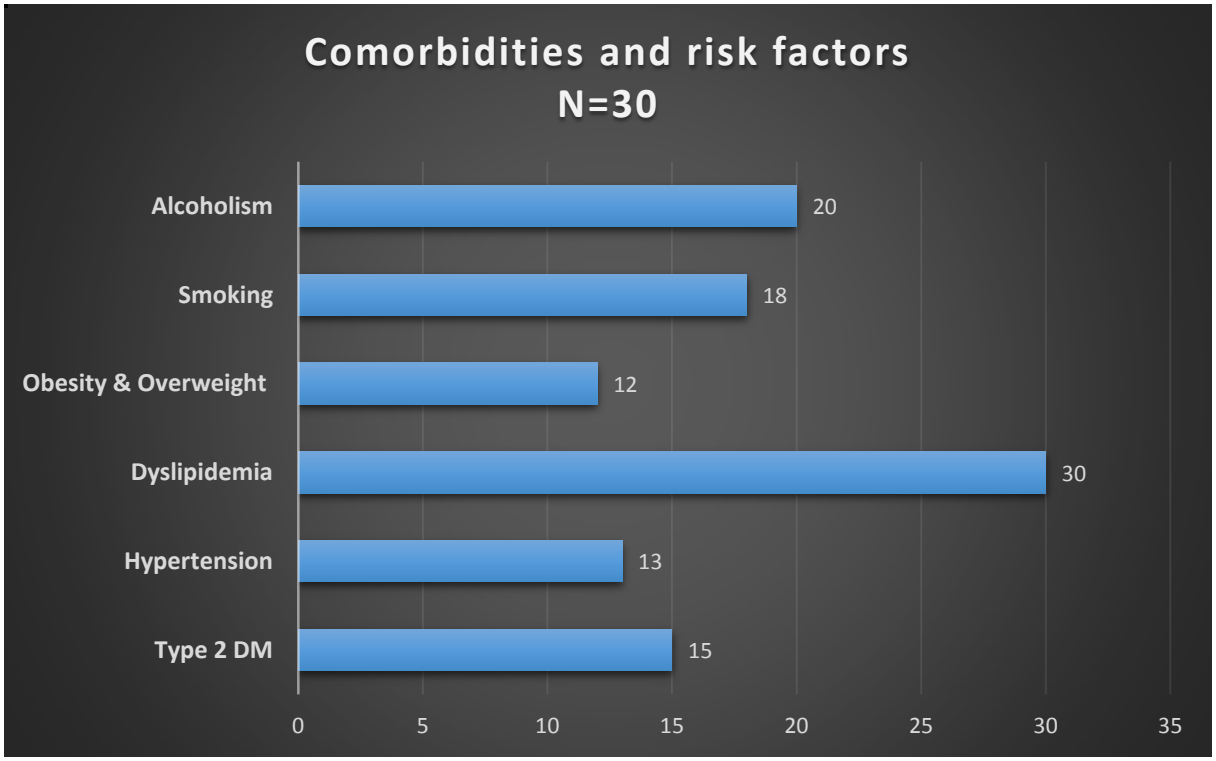
## Results

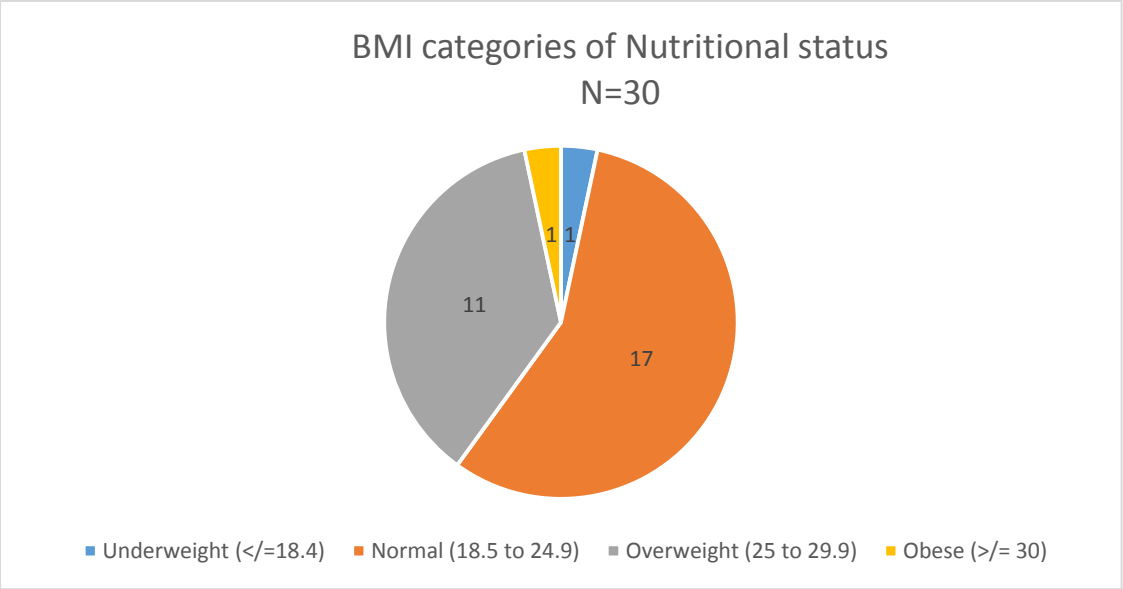
**Central tendency characteristics of Age and BMI of study participants**

| S. No. | Variables | Minimum | Maximum | Mean | Std. Deviation | Median |
|---|---|---|---|---|---|---|
| 1. | Age | 33 | 63 | 49.03 | 10.45 | 46 |
| 2. | BMI | 18.2 | 32.1 | 24.58 | 3.29 | 24.05 |

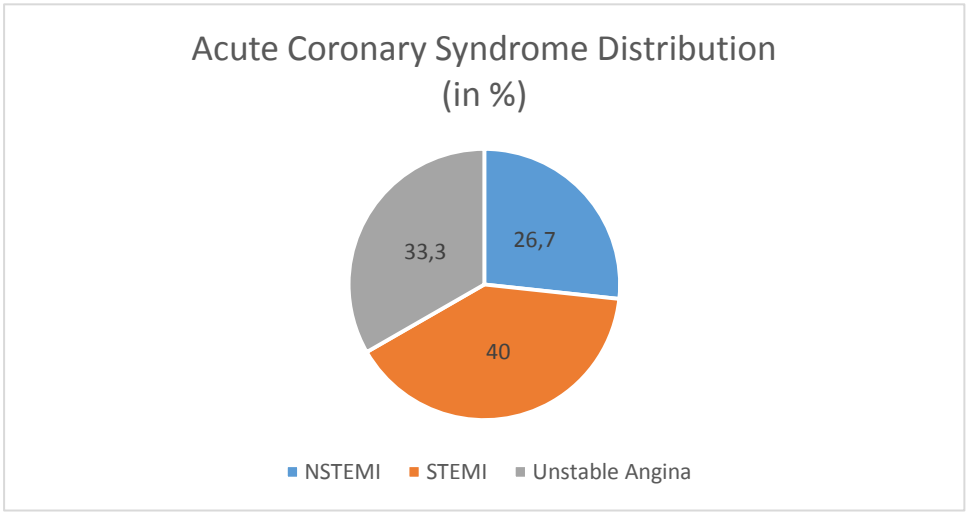


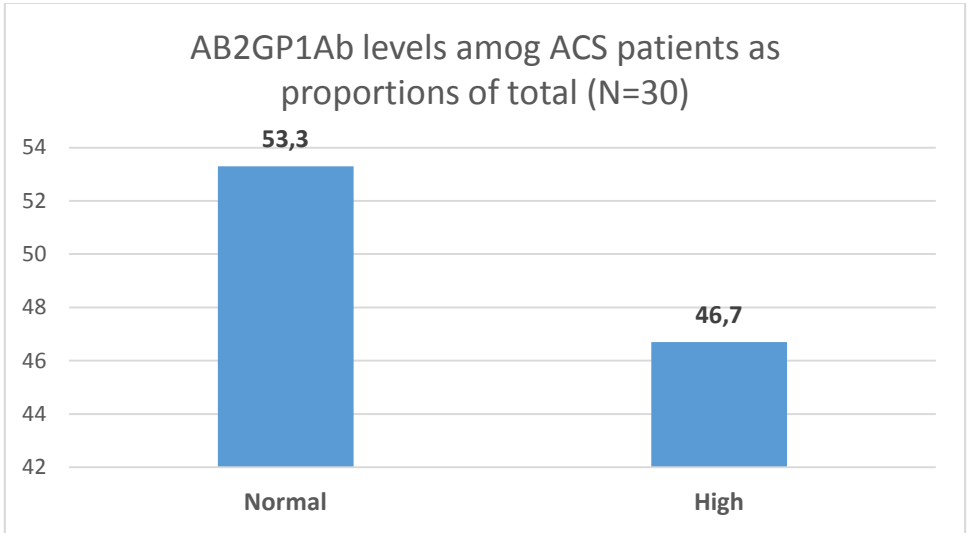

Mean Age of the participants was 49.03 (+/-10.45s.d.) and mean BMI of participants was 24.58 (+/-3.29 s.d.). Females constituted only 13.3% of the participants and males were 86.7 percentage. Participants above 40 and below 60 years of age were in a majority (73.3%) and above 60 years participants were only 16.7% and only 10% were below 40 years of age.






Alcohol consumption and smoking were prevalent among 66.7% and 60% of patients respectively. Obesity and overweight patients constituted around 40% of participants. Dyslipidemia was present in all 30 study participants. Among the ACS patients taking part in the study 50% were diabetic and 43.3% were hypertensive.



STEMI patients were 40% followed by Unstable Angina (33.3%) and NSTEMI (26.7%). High levels of AB2GP1Ab levels were found in 46.7% ACS patients,

| Variables | ANTI-BETA2 GLYCOPROTEIN1 ANTIBODY LEVELS N=30 | | $\chi^2$ value | p value |
|---|---|---|---|---|
| | Normal (%) n = 16 | High (%) n = 14 | | |
| STEMI | | | | |
| No | 11 (61.1) | 7 (38.9) | 1.094 | 0.296 |
| Yes | 5 (41.7) | 7 (58.3) | | |
| NSTEMI | | | | |
| No | 10 (45.5) | 12 (54.5) | 2.058 | 0.151 |
| Yes | 6 (75) | 2 (25) | | |
| Unstable Angina | | | | |
| No | 11 (55) | 9 (45) | 0.067 | 0.796 |
| Yes | 5 (50) | 5 (50) | | |

More than half (58.3%) of the STEMI patients had high levels of AB2GP1 IgA antibody. About 25% of NSTEMI and 50% of unstable angina patients had high levels of AB2GP1 IgA antibody.

| Variables | ANTI-BETA2 GLYCOPROTEIN1 ANTIBODY LEVELS N=30 | | $\chi^2$ value | p value |
|---|---|---|---|---|
| | Normal (%) n = 16 | High (%) n =14 | | |
| Age Category | | | | |
| Less than 50 years | 8 (47.1) | 9 (52.9) | 0.621 | 0.431 |
| 50 years or more | 8 (61.5) | 5 (38.5) | | |
| Gender | | | | |
| Female | 3 (75) | 1 (25) | 0.871 | 0.351 |
| Male | 13 (50) | 13 (50) | | |

Half of the male patients and 52.9% of those less than 50 years had high levels of AB2GP1 IgA antibody.

| Variables | ANTI-BETA2 GLYCOPROTEIN1 ANTIBODY LEVELS N=30 | | $\chi^2$ value | p value |
|---|---|---|---|---|
| | Normal (%) n = 16 | High (%) n = 14 | | |
| Smoking | | | | |
| No | 8 (66.7) | 4 (33.3) | 1.429 | 0.232 |
| Yes | 8 (44.4) | 10 (55.6) | | |
| Alcohol | | | | |
| No | 6 (60) | 4 (40) | 0.268 | 0.605 |
| Yes | 10 (50) | 10 (50) | | |
| SHTN | | | | |
| No | 8 (47.1) | 9 (52.9) | O.621 | 0.431 |
| Yes | 8 (61.5) | 5 (38.5) | | |
| T2DM | | | | |
| No | 9 (60) | 6 (40) | 0.536 | 0.464 |
| Yes | 7 (46.7) | 8 (53.3) | | |
| BMI Category | | | | |
| Normal | 8 (44.4) | 10 (8.4) | 1.429 | 0.232 |
| Obese or overweight | 8 (66.7) | 4 (33.3) | | |
| | | | | |

Among co-morbidities and other risk factors 53.3% of T2DM and 38.5% of SHTN patients had high levels of AB2GP1Ab. Similarly 50% of those with alcohol consumption and 55.6% of those who smoke were also found to have high levels of AB2GP1 IgA antibody. But as the study was involving a small sample size none of these associations (even those in the earlier tables) were found to be statistically significant ($p>0.05$).

**Discussion**

The pathophysiological basis of ACS relies on the existence of vulnerable atherothrombotic plaques within the coronary arteries[1]. These plaques become unstable due to plaque rupture or the local escalation of thrombotic events[1].In isolated human atherosclerotic plaques, Beta2 glycoprotein is localized in the sub endothelial region and in intimal–medial borders[1].

The relation betweenBeta2 glycoprotein and atherosclerosis is intriguing[2]. Atheromas containBeta2 glycoprotein[2]. Our study raises the possibility that anti-beta2 glycoprotein 1 antibodies may be associated with the risk of acute myocardial infarction. Antibodies to Beta2 glycoprotein1 have been shown to enhance the accumulation of oxidized LDL into macrophages[3].This mechanism may be important in the development of atherosclerosis in patients with antibodies to Beta2 glycoprotein1[3,9].Antibodies to Beta 2 glycoprotein1 have been found to increase coagulation by humoral mechanisms (via the coagulation cascade and plasminogen system) and by increasing platelet adhesiveness, which may enhance acute events in CAD[5].The two hit hypothesis has been proposed to be a good model for the pathogenesis of Antiphospholipid syndrome[6]. Yet, it cannot clarify why antiphospholipid antibodies present in healthy individuals are not pathogenic. It is proposed that a “first-hit” injury primes the endothelium, and a “second-hit” injury triggers thrombus formation. Studies have shown that anti-beta2 glycoprotein1 antibodies infused into mice only initiate thrombus formation following vessel-wall injury[10,11]. Endothelium priming involves vessel-wall injury, infection, recent surgery[6]. Once primed, the “second-hit” injury, such as smoking, immobilisation, pregnancy, malignancy, etc., stimulates the development of thrombosis[6].Anti-beta2 glycoprotein1 antibodies abrogate the inhibitory function of the Beta2 glycoprotein1 on platelet aggregation and adhesion triggered by the active conformation of von Willebrand factor[8]. Moreover, in a number of patients with the Antiphospholipid syndrome and a history of thrombosis, anti-beta2 glycoprotein1 antibodies were associated with the presence in plasma of increased levels of von Willebrand factor and so elevated prothrombotic function[12]. In this way, anti-beta2 glycoprotein1 antibodies may enhance thrombus formation at the site of plaque rupture (atherothrombosis) rather than directly contributing to plaque formation[8]. An additional role may be the potential ability of anti-beta2 glycoprotein1 antibodies to reduce plaque stability by promoting the local inflammatory process, as recently demonstrated in an experimental model [13].

We found significantly increased levels of IgA anti-beta2 glycoprotein1 antibodies in all ACS patients, as well as in patients with UA and STEMI. However, in an earlier study, we found a strong relationship between increased IgAanti-beta2 glycoprotein1 antibody levels and several thromboembolic manifestations[14].Farsi et al. also detected anti-beta2 glycoprotein1 antibodies in a large proportion (29.7%) of coronary artery disease (CAD) patients and in only 2.5% of controls[15].However, further studies on larger, selected ACS population are needed to understand the involvement of antiphospholipid antibodies in CAD and ACS.

**Conclusion**

The data from our study support the potential importance and prognostic implications of antiphospholipid antibody testing in patients with acute coronary syndrome. As the search for newer

biomarkers for cardiovascular disease increases their use may add to standard risk assessment and treatment outcomes. Whether testing for antiphospholipid antibodies, especially antibodies to beta2 glycoprotein1 will strengthen the bridge between diagnostic, prognostic and treatment modalities for CAD and its complications warrants larger prospective studies.

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