



ORIGINAL ARTICLE

## Frequency of low HDL-C levels in patients suffering from acute coronary syndrome.

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**Article Citation:** Yasir M, Ahmad M, Goher F, Andleeb M. Frequency of low HDL-C levels in patients suffering from acute coronary syndrome. Professional Med J 2025; 32(07):1801-1808. <https://doi.org/10.29309/TPMJ/2025.32.12.9768>

**ABSTRACT... Objective:** To find out how often patients with acute coronary syndrome have low HDL-c values. **Study Design:** Cross-sectional study. **Setting:** Department of Cardiology, Faisalabad Institute of Cardiology, Faisalabad. **Period:** 29<sup>th</sup> May 2021 to 28<sup>th</sup> November 2021. **Methods:** Patients taking lipid lowering drugs, pregnant females and familial hyperlipidemia were excluded. Early morning fasting lipid profile along with HDL-c level was sent to hospital pathology lab. The reports were collected and interpreted by the researcher himself as per operational definition. Frequency of low HDL-c in patients of ACS was noted. **Results:** A total of 384 patients presenting in emergency with acute coronary syndrome of age 30-80 years of either gender were included. Age range in this study was from 30 to 80 years with mean age of  $57.51 \pm 7.50$  years. Majority of the patients 248 (64.58%) were between 56 to 80 years of age. Out of the 384 patients, 227 (59.11%) were male and 157 (40.89%) were females with male to female ratio of 1.4:1. Mean BMI was  $30.67 \pm 3.72$  kg/m<sup>2</sup>. Frequency of low HDL-c levels in patients suffering from acute coronary syndrome was found in 172 (44.79%) patients. **Conclusion:** This study demonstrated that many of patients suffering from acute coronary syndrome have a low frequency of low HDL c levels.

**Key words:** Acute Coronary Syndrome, High Density, Lipoprotein.

### INTRODUCTION

Cardiovascular disease (CVD) remains the cause of morbidity and mortality worldwide and is the leading cause of mortality for both men and women.<sup>1</sup> Patients with suspected acute coronary syndrome (ACS) >20 million presents to emergency rooms in North America and Europe are a substantial population in emergency rooms across the globe.<sup>2</sup> Forty-six point eight percent of emergency presented patients with acute coronary syndrome.<sup>3</sup>

Acute coronary syndrome (ACS) denotes a clinical presentation ranging from that of unstable angina to non ST segment elevation myocardial infarction (NSTEMI) to ST segment elevation myocardial infarction (STEMI). In terms of pathology, nearly always the ACS is associated with partial or total thrombosis of the artery supplying the infarct or the rupture of atherosclerotic plaque. But stable coronary artery disease (CAD), when physiologic stress (trauma, blood loss, anemia, infection, or tachyarrhythmia) escalates demands on the heart, can occasionally result in ACS without

plaque rupture and thrombosis. The subtypes of coronary artery disease (CAD) include acute coronary syndrome (ACS) and stable coronary artery disease (CAD), including or excluding angina.

Although the anatomical backgrounds of stable CAD and ACS are similar, their pathophysiologies differ significantly. Risk factors such as high blood pressure, high cholesterol, smoking, diabetes, and heredity can accelerate inflammatory pathways, which are thought to be significant contributors to plaque disruption and thrombosis.<sup>4</sup>

There are smoking, dyslipidemia, diabetes mellitus, and hypertension as the main modifiable risk factors and a positive family history of the disease is the non-modifiable risk factor in our local community.<sup>5</sup> Strong evidence from several epidemiological studies confirms that high density lipoprotein (HDL) cholesterol (HDL-C) content is independently and negatively correlated with atherosclerotic cardiovascular disease.<sup>6</sup>

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**Article received on:** 14/04/2025  
**Accepted for publication:** 17/06/2025

The presence of low plasma HDL levels has a very strong association with an increased risk of developing coronary artery disease, particularly in that of premature coronary atherosclerosis, implying a protection of coronary artery disease by high density lipoproteins. Population based research suggests that every 1 mg/dl drop in the high density lipoprotein cholesterol levels, is associated with a risk of future cardiovascular events of 2% to 3%.<sup>7</sup>

A mean age of  $55.720 \pm 8.901$  years was found in local research 7. Of the patients, around 38% were female and 62% were male. Roughly 20% of individuals experienced unstable angina, 9% experienced NSTEMI, and 71% experienced STEMI. Of all patients admitted with ACS, approximately 48% had poor high density lipoproteins.

Means age was  $55.720 \pm 8.901$  years. Seven (9%) had NSTEMI, about 71 per cent had STEMI, and about 20 per cent had unstable angina. Patients studied were of both sex (38 % female and 62 % male).<sup>7</sup> About 48% of ACS patients hospitalized had low quality HDLs.

## METHODS

This cross-sectional study was conducted in the Department of Cardiology, Faisalabad Institute of Cardiology, Faisalabad, from 29th May 2021 to 28th November 2021 after approval from ethical review committee No. 13/DME/FIC/FSD, dated: 23-12-2020. A sample size of 384 cases was calculated using OpenEpi software with a 95% confidence level, 5% absolute precision, and an expected prevalence of low HDL-C at 48% in patients with acute coronary syndrome (ACS). A non-probability consecutive sampling technique was employed. Inclusion criteria included patients of both genders, aged 30 to 80 years, presenting with ACS in the emergency department. Exclusion criteria comprised patients on lipid-lowering agents, those with familial hyperlipidemia, pregnant women, and individuals who did not provide consent. Following ethical approval, eligible patients were enrolled, and written informed consent was obtained. Data on demographics, symptom duration, smoking,

diabetes, hypertension, obesity, and family history of ACS were recorded. Patients were treated according to hospital protocols, and early morning fasting lipid profiles, including HDL-C levels, were obtained from the hospital pathology lab. The results were interpreted by the researcher, and the frequency of low HDL-C in ACS patients was documented using a structured proforma.

## Data Analysis Procedure

Data was entered on computer software, SPSS version 22. Mean and standard deviation of quantitative data such as age and level of HDL-c and frequency and percentages of qualitative data such as gender, diabetes, hypertension, smoking, obesity, and presence of low HDL-c were presented. To control for effect modifiers, data was stratified on variables such as age, gender, BMI ( $> 25\text{Kg/m}^2$ ,  $< 25\text{Kg/m}^2$ ), diabetes, hypertension, smoking and family history of ACS. The significance was checked with  $P \text{ value} \leq 0.05$  for significant using post stratification Chi square test.

## RESULTS

The study included 384 patients with acute coronary syndrome (ACS), with a mean age of  $57.51 \pm 7.50$  years. The majority of participants were aged between 56 and 80 years (64.58%), while 35.42% were aged 30 to 55 years. Of the participants, 59.11% were male and 40.88% were female. Regarding body mass index (BMI), 86.72% had a BMI greater than  $25 \text{ kg/m}^2$ , while 13.28% had a BMI of  $25 \text{ kg/m}^2$  or lower, with a mean BMI of  $30.67 \pm 3.72 \text{ kg/m}^2$ . A positive family history of coronary artery disease was reported by 38.8% of participants. Common confounding factors included hypertension (58.85%), diabetes mellitus (48.96%), and smoking (45.57%). The frequency of low HDL-C levels was observed in 44.79% of patients, while 55.20% had normal HDL-C levels. Table-I

Table-II highlighted significant associations between low HDL-C levels and various demographic and clinical parameters among patients with Acute Coronary Syndrome (ACS). Participants aged 56-80 years were more likely to have low HDL-C levels (73.84%) compared to

those aged 30-55 years (26.16%) ( $p = 0.001$ ). Males exhibited a markedly higher prevalence of low HDL-C levels (87.21%) than females (12.79%) ( $p = 0.0001$ ). BMI  $>25$  kg/m<sup>2</sup> was strongly associated with low HDL-C levels (79.07%,  $p = 0.0001$ ). A family history of ACS was present in 79.07% of participants with low HDL-C levels, compared to only 6.13% in those without ( $p = 0.0001$ ). Hypertension was less common among participants with low HDL-C levels (39.53%) than those without (74.53%) ( $p=0.0001$ ), while diabetes mellitus (77.33% vs. 25.94%) and smoking (65.70% vs. 29.25%) were significantly more prevalent in the low HDL-C group ( $p=0.0001$  and  $p=0.001$ , respectively). These

findings underscore the multifaceted relationship between low HDL-C levels and adverse clinical and demographic factors in ACS patients.

## DISCUSSION

One of the main blood carriers of cholesterol is high-density lipoprotein, or HDL. Unlike other lipoproteins, HDL has numerous physiological roles that positively impact the circulatory system unless HDL is altered pathologically, which is why it garners special attention. The anti-inflammatory and antioxidant properties of HDL are among its recently highlighted functions. Protection against cardiovascular disease is linked to HDL's strong anti-oxidant and anti-inflammatory properties.<sup>8</sup>

| Parameter                | Category                           | No. of Patients | %      |
|--------------------------|------------------------------------|-----------------|--------|
| Age (in years)           | 30-55                              | 136             | 35.42% |
|                          | 56-80                              | 248             | 64.58% |
| Mean age $\pm$ SD        | 57.51 $\pm$ 7.50 years             |                 |        |
| Gender                   | Male                               | 227             | 59.11% |
|                          | Female                             | 157             | 40.88% |
| BMI (kg/m <sup>2</sup> ) | $\leq 25$                          | 51              | 13.28% |
|                          | $> 25$                             | 333             | 86.72% |
| Mean BMI $\pm$ SD        | 30.67 $\pm$ 3.72 kg/m <sup>2</sup> |                 | NA     |
| Family History           | Positive                           | 149             | 38.8%  |
| Confounding variables    | Hypertension                       | 226             | 58.85% |
|                          | Diabetes mellitus                  | 188             | 48.96% |
|                          | Smoking                            | 175             | 45.57% |
| Low HDL-c levels         | Yes                                | 172             | 44.79% |
|                          | No                                 | 212             | 55.20% |

**Table-I. Demographic and clinical characteristics of study participants (n = 384)**

| Parameter                | Category  | Yes (n = 172) | No (n = 212) | P-Value |
|--------------------------|-----------|---------------|--------------|---------|
| Age (years)              | 30-55     | 45 (26.16%)   | 91 (42.92%)  | 0.001   |
|                          | 56-80     | 127 (73.84%)  | 121 (57.08%) |         |
| Gender                   | Male      | 150 (87.21%)  | 77 (36.32%)  | 0.0001  |
|                          | Female    | 22 (12.79%)   | 135 (63.68%) |         |
| BMI (kg/m <sup>2</sup> ) | $\leq 25$ | 36 (20.93%)   | 15 (7.08%)   | 0.0001  |
|                          | $> 25$    | 136 (79.07%)  | 197 (92.92%) |         |
| Family history of ACS    | Yes       | 136 (79.07%)  | 13 (6.13%)   | 0.0001  |
|                          | No        | 36 (20.93%)   | 199 (93.87%) |         |
| Hypertension             | Yes       | 68 (39.53%)   | 158 (74.53%) | 0.0001  |
|                          | No        | 104 (60.47%)  | 54 (25.47%)  |         |
| Diabetes Mellitus        | Yes       | 133 (77.33%)  | 55 (25.94%)  | 0.0001  |
|                          | No        | 39 (22.67%)   | 157 (74.06%) |         |
| Smoking                  | Yes       | 113 (65.70%)  | 62 (29.25%)  | 0.001   |
|                          | No        | 59 (34.30%)   | 150 (70.75%) |         |

**Table-II. Distribution of demographic and clinical parameters among participants with and without low HDL-C levels (n = 384)**

A lower risk of coronary heart disease (CHD) is positively correlated with high-density lipoprotein (HDL). According to the Adult Treatment Panel III guidelines of the US National Cholesterol Education Program, an HDL cholesterol level (HDL-C) of 60 mg/dL or more is considered a negative (protective) risk factor. Executive Summary of the National Cholesterol Education Program's Third Report (NCEP).<sup>9</sup> Conversely, a level of HDL cholesterol below 40 mg/dL is considered high-risk. Interventions to increase HDL cholesterol levels have been linked to fewer CHD occurrences, according to randomized, controlled clinical trials.

Across a range of low-density lipoprotein-cholesterol (LDL-C) values, baseline HDL-C level was consistently and inversely associated with incident coronary and coronary vascular disease events, according to a prospective analysis by Mora et al.<sup>10</sup> that examined the relationship between cholesterol and cardiovascular events in women.<sup>10</sup> Although there is a correlation between cardiovascular health and greater HDL levels, there is no evidence that a little increase in HDL improves health. To put it another way, whereas elevated HDL levels may be associated with improved cardiovascular health, raising HDL levels alone may not improve cardiovascular health.<sup>11</sup>

The risk of heart disease increases tenfold for a given amount of LDL when HDL fluctuates from high to low, according to data from the seminal Framingham Heart Study. On the other hand, when HDL levels fluctuate from low to high, the risk increases threefold. Meyers and associates<sup>12</sup> insufficiently high HDL levels put even those with extremely low LDL levels at greater risk. When is it appropriate to start treatment for high cholesterol?<sup>13,14</sup> Even in those with normal levels of total and LDL cholesterol, HDL levels below 40 mg/dL increase the risk of coronary artery disease. HDL values in the range of 40 to 60 mg/dL are regarded as "normal." Richard NF and others.<sup>15</sup>

On the other hand, HDL levels above 60 mg/dL might actually shield individuals from heart

disease. It's true that doctors have known for a while that the greater the HDL levels, the better. Insufficient HDL-C For men, levels of less than 40 mg/dl (1.0 mmol/L) and for women, less than 50 mg/dl (1.3 mmol/L) were defined by Grundy SM et al.<sup>16</sup> and Alberti KG et al.<sup>17</sup> In patients with ACS, low HDL-C concentrations are a sign of a bad prognosis, similar to the risk linked to low HDL in patients with chronic CVD. One prominent example, though not the only one, is the MIRACL clinical study (Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering), which randomized 3086 ACS patients to receive either atorvastatin or a placebo for 16 weeks.

The probability of death, recurrent angina, or repeat infarction at 16 weeks was predicted by HDL-C levels at the time of ACS diagnosis in a treatment-adjusted analysis (Olsson AG et al.<sup>18</sup>). Low-density lipoprotein cholesterol (LDL-C) levels did not really predict CVR; however, patients in the upper quartile of HDL-C (>53 mg/dL) had a 62% reduced risk than those in the lower quartile (>\_38 mg/dL). Multivariate analysis revealed that patients with low HDL-C had a higher risk of dying or experiencing a cardiovascular event at one month and one year of follow-up in a single-center observational study of 1032 ACS patients who received PCI and statin treatment. RM Wolfram et al.<sup>19</sup>

A different study that included 320 individuals who were enrolled at the time of the ACS diagnosis revealed that a lower cardiovascular risk was linked to high HDL-C levels. Tziakas DN and others.<sup>20</sup>

The majority of case-control and prospective observational studies show that low HDL is an independent risk factor for CAD. On the other hand, high HDL levels are linked to longevity and offer protection against the onset of atherosclerosis. The Framingham Study shows that as HDL levels gradually drop below 40 mg/dL, the risk for CAD rises significantly. WP Castelli et al.<sup>21</sup>, Numerous mechanisms have been discovered via which HDL prevents the development of CVD. As previously mentioned, RCT is a known antiatherogenic property of HDL. The reduction

of inflammation via the selective elimination of endothelial cell adhesion molecules, which enable the binding of mononuclear cells to the artery wall and encourage the development of lesions, is a second significant mechanism.<sup>22</sup>

An investigation involving 6,266 patients from the Middle East in six Gulf nations Low HDL (62%) and adequate HDL (38%), according to Khalid AR et al.<sup>23</sup>, were prevalent. and align with a U.S. research Among 8,500 males at Veterans Affairs Medical Centers across the United States, 63% had low HDL-C, according to Rubins et al.<sup>24</sup> In contrast to the data above, which indicate a relatively high prevalence of low HDL\_C, several studies from various Middle Eastern provinces have indicated high prevalence; however, a research conducted by Ibrahim AZ et al.<sup>25</sup> in Oman on 1,458 patients revealed a lower frequency of low HDL\_C (53%).

Additionally, a study conducted on 367 individuals in Spain by Xavier P et al.<sup>26</sup> found a significant prevalence of low HDL\_C (57%) to a lesser extent. Additionally, a study by Sachdeva A et al.<sup>27</sup> on 136,905 patients in the USA revealed that decreased HDL-C was present in 55% of patients admitted with CAD. Additionally, another similar study conducted on 1,032 individuals in the USA by Wolfram M et al.<sup>28</sup> revealed a predominance of low HDL\_C (53.3%).

On the other hand, some research revealed a low prevalence of HDL. Arai et al.<sup>29</sup> found that 249 patients in Japan had a high prevalence of good HDL (66%) and low HDL (34%). Additionally, Correia et al.<sup>30</sup> in Brazil found that 72% of patients had adequate HDL and 28% of patients had poor HDL. The small number of patients, poor eating habits, obesity prevalence, poor sport culture, high prevalence of direct or passive smoking, and poor health culture are the reasons for the higher percentage of low HDL\_C and low percentage of satisfactory HDL\_C in this study compared to all other studies conducted overseas.

A 12- to 14-hour fast was followed by the collection of all blood samples from ACS patients in the MIRACL investigation, which shown that low HDL-C levels predicted the probability of

recurrent cardiovascular events over the next 16 weeks.<sup>31</sup> Similarly, samples obtained during an overnight fasting state likewise yielded the low HDL-C levels linked to a considerably greater risk of in-hospital death in Asian STEMI patients who underwent successful PCI.<sup>130</sup> In the four days following an ACS event, there was comparatively minimal variation in HDL-C levels, according to the LUNAR study, which concentrated on the timing of sample collection.<sup>32</sup>

It is still unclear why low HDL-C levels are associated with a poor short-term prognosis in ACS patients. Several analyses of ACS patient data have revealed an inverse correlation between the HDL-C level and the rate of multi-vessel coronary disease in terms of angiographic results.<sup>33-37</sup> Furthermore, ACS patients with low HDL-C levels were more likely than those without to have severe heart failure.<sup>33</sup> These findings imply that the degree of coronary artery disease and the deterioration of cardiac hemodynamics due to multi-vessel coronary disease are related to a low HDL-C level.

## CONCLUSION

This study concluded that there is high frequency of low HDL-c levels in patients suffering from acute coronary syndrome. So, we recommend that early recognition and management of this condition should be done in order to reduce the mortality and morbidity of community. Also public awareness programs should be arranged on national and regional levels for early screening and treatment of low HDL-c levels in order to reduce cerebrovascular accidents (CVA) and their complications.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## SOURCE OF FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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| 1                                       | Muhammad Yasir: Study design and synopsis. |
| 2                                       | Munir Ahmad: Data analysis.                |
| 3                                       | Fozia Goher: Manuscript writing.           |
| 4                                       | Maria Andleeb: Data collection.            |