RESEARCH ARTICLE

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# MONOCYTE TO HDL RATIO AS A SHORT-TERM PROGNOSTIC MARKER IN PATIENTS WITH ACUTE CORONARY SYNDROME AND ITS CORRELATION WITH THROMBOLYSIS IN MYOCARDIAL INFARCTION (TIMI) SCORE AND ANGIOGRAPHIC PROFILE

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### **ABSTRACT:**

**BACKGROUND:** Acute Coronary Syndrome (ACS) is a gamut of clinical conditions which occurs due to imminent, decreased blood flow to myocardial musculature. The MHR, monocyte to HDL-c ratio is a newly originated marker is based on inflammatory activity. MHR has been proposed as the latest predictor and prognostic index of acute coronary syndrome and other cardiovascular diseases. <sup>12,13</sup> This study was conducted to assess the prognostic significance of the Monocyte to HDL ratio in ACS patients.

MATERIALS AND METHODS: A total of 41 Patients who were diagnosed with Acute Coronary syndrome without any exclusion criteria were taken in the study. Once the patients were clinically diagnosed with Acute Coronary syndrome using ECG and cardiac panel, a complete history was elicited by the doctor as the principal author as an observer. Later investigations such as CBC, Lipid Profile, echo, and angiography were carried out at the prescribed times. Risk assessment was done for every patient using the TIMI risk assessment score. Along with the data on detailed clinical history, patients' residential address and contact numbers of the patient and emergency contact was recorded. The patients were consulted over call every month till the end of the study.

**RESULTS**: The age of the study samples ranged from 36 years to 67 years. The average age of the patients was  $54.07\pm7.31$  years. The average TIMI score obtained for the study population was  $2.731\pm1.09$ . A TIMI score of more than one was obtained among 92.6% of the study population. Maximum patients (36.5%) obtained a TIMI score of 2. The average MHR was  $19.62\pm6.92$ . MHR value is 74.6% in correlation with the TIMI score. At a cut off value of 23.75 the sensitivity and specificity of MHR for MACE were 87.5% and 88%.

**CONCLUSION:** MHR is a new cost-effective, logical and good predictive marker for coronary vascular diseases. Multiple studies have emphasized the utilization and findings relating to MHR. MHR can be used as a good prognostic factor for the short term, among patients with Acute Coronary syndrome.

**Keywords:** Acute Coronary Syndrome (ACS), monocyte to HDL-c ratio (MHR), Thrombolysis in Myocardial Infarction (TIMI)

#### INTRODUCTION:

Acute Coronary Syndrome (ACS) is a gamut of clinical conditions which occurs due to imminent, decreased blood flow to myocardial musculature. ACS is a more generic word that comprises mostly Myocardial ischemia, unstable angina, and sudden cardiac death. The myocardial ischemia can be either STEMI or NSTEMI. STEMI refers to ST-elevated Myocardial infarction. NSTEMI represents non-ST-elevated myocardial ischemia. The world is amidst an epidemiological transition in which non-communicable diseases are not only a public health emergency among developed countries but also gaining to be as significant as communicable diseases and malnutrition among developing countries. Cardiovascular disease is a significant global public health problem. Cardiovascular diseases are the major cause of global mortality. Cardiovascular diseases contribute to ten percent of the burden of the disease of the world. Cardiovascular disease contributes to 32% of the global total mortality.<sup>1,2</sup> In the year 2019, approximately 17.9 million deaths occurred due to Coronary vascular diseases. Most of the deaths were contributed by developing and underdeveloped nations.<sup>3</sup> 38% of the premature deaths in 2019 were caused by cardiovascular diseases. It is important to establish a diagnosis for symptomatic patients at the earliest to begin essential interventions to decrease morbidity and mortality. There are numerous innovations in antithrombotic and reperfusion therapy for myocardial ischemia in the last 2 decades. 4 Yet the prognosis and outcome of cases with ACS remain poor. The need for a new biomarker for better assessment of the prognosis of acute coronary syndrome patients has been suggested by multiple studies. In the atherosclerotic disease process, the role of inflammation was well established in the early 2000s. Since then, the association of CRP and IL-6 with the severity of the disease progression and prognosis among Acute coronary syndrome patients was established in multiple studies. The role of monocyte in the promotion of inflammation is well established. The inflammatory activity of monocytes in platelets and endothelial cells is a prothrombotic phenomenon.<sup>8</sup> Studies have established that increased monocyte count is a poor prognostic factor for acute coronary syndrome patients and increased the probability of another episode. <sup>8</sup> Just the opposite is the role of High-density lipoprotein. In addition to its role in reverse cholesterol transport (RCT), the HDL-C molecules resist the migration of macrophages to the inflammatory site. It stops the oxidation of LDL molecules by monocytes. In addition to this macrophage, RCT is considered the "holy grail" of ACS treatment. Via ABCG1 transporter mature high-density lipoprotein causes efflux of cholesterol from macrophages. 10,11

The MHR, monocyte to HDL-c ratio is a newly originated marker is based on inflammatory activity. MHR has been proposed as the latest predictor and prognostic index of acute coronary syndrome and other cardiovascular diseases. <sup>12,13</sup> This study tries to assess the prognostic significance of the Monocyte to HDL ratio in ACS patients.

#### **Materials and Methods:**

This observational analytical study was conducted in the department of General Medicine at a tertiary care centre between the period of Feb-2020 to March 2020. Patients who were diagnosed with Acute Coronary syndrome without any exclusion criteria were taken. A total of 52 patients were diagnosed with Acute Coronary syndrome during the study period. Out of the 52 patients, 11 did not satisfy the criteria for inclusion and were not included in the study. The study concluded with 41 patients.

Once the patients were clinically diagnosed with Acute Coronary syndrome using ECG and cardiac panel, a complete history was elicited by the doctor as the principal author as an observer. Later

investigations such as CBC, Lipid Profile, echo, and angiography were carried out at the prescribed times. Risk assessment was done for every patient using the TIMI risk assessment score. Along with the data on detailed clinical history, patients' residential address and contact numbers of the patient and emergency contact was recorded. The patients were consulted over call every month till the end of the study. The study concluded with 41 patients.

# **RESULTS**

The age of the study samples ranged from 36 years to 67 years. The average age of the patients was  $54.07\pm7.31$  years. 65.8% of the study population were males and 34.2% of the study population were female. The ratio of male: female in the study was 1.9:1. Mean age among men  $-51.85\pm7.1$  years. Mean age among women- $58.25\pm5.2$  years., premature ACS was observed among 85.7% of females in the study and 70% among the male participants. 77.5% of the total study population had premature Acute Coronary Syndrome. 51% of the study population had a positive smoking history. The average BMI of the patient was found to be  $28\pm5.30$  kg/m². 29.26% of the study population. The average waist circumference for the entire study population was  $88.10\pm7.72$  cms. 56% of the study population had a family history of coronary artery diseases. The average systolic blood pressure among the study population was  $152\pm15$  mmHg. The average diastolic blood pressure among the study population was  $107\pm12$  mmHg. 36 were hypertensive at the time of presentation. 12 patients were diagnosed as non-ST-segment elevated myocardial infarction, 25 patients were diagnosed as ST-segment elevated Myocardial Infarction and 4 patients were diagnosed as Unstable Angina. The average TIMI score obtained for the study population was  $2.731\pm1.09$  & the average MHR was as shown in Table 1

TABLE 1: BASELINE CLINICAL CHARACTERISTICS:

variable	Frequency (n=41)/	Percentage
	Mean ± SD	
Age (Years)		
$Mean \pm SD$	54.07 <b>±</b> 7.31	
Sex		
Male		65.8 %
Female		34.2 %
BMI (kg/m <sup>2)</sup>	28±5.30	
waist circumference	88.10±7.72	
Systolic B.P (mm Hg)	152±15	
Diastolic B.P (mm Hg)	107±12	
Hypertension	36	88%
Smoking	21	51%
Family history of CAD	23	56%
Premature acute coronary syndrome		77.5%
Diagnosis		
NSTEMI	12	29%
STEMI	25	61%
Unstable Angina	4	10%
TIMI Score	2.731±1.09	
MHR	19.62±6.92	
Angiography profile		
Single vessel stenosis	13	32%
Double vessel stenosis	20	49%
Triple vessel stenosis	8	19%

The average creatinine among the study subjects was  $0.83\pm0.14$ . The average Egfr among the study subjects was  $101\pm12$ . Average Fasting Blood Sugar among the study subjects was  $86.82\pm18.99$  mg/dl. The average HDL-c among the study subjects was  $35\pm5$  mg/dl. The average LDL among the study subjects was  $161\pm14$  mg/dl. Average LDL: HDL among the study subjects was  $4.58\pm2.62$ . The average WBC count of the study population was  $11577\pm2351$  cells/mm<sup>3</sup>. The average monocyte count among the study population was  $662\pm183$ /mm<sup>3</sup> The average neutrophil and lymphocyte count of the study population is  $5043\pm1173$  and  $5370\pm1153$  respectively as shown in Table 2

TABLE 2: LABORATORY CHARACTERISTICS

variable	$Mean \pm SD$
Serum creatinine (mg/dl)	0.83±0.14
eGFR (ml/min)	101±12
Fasting Blood sugar (mg/dl)	86.82±18.99
HDL-C (mg/dl)	35±5
LDL-C (mg/dl)	161±14
LDL : HDL (mg/dl)	4.58±2.62
Total Cholesterol (mg/dl)	360±17
WBC count (/mm <sup>3)</sup>	11577±2351
Monocyte count (/mm <sup>3)</sup>	662±183
Neutrophil count (/mm <sup>3)</sup>	5043±1173
Lymphocyte count (/mm <sup>3)</sup>	5370±1153

Patients can be categorized into five categories based on TIMI score. A TIMI score of more than one was obtained among 92.6% of the study population. Maximum patients (36.5%) obtained a TIMI score of 2 as shown in Table 3

TABLE 3: CATEGORISATION OF PATIENTS BASED ON TIMI SCORE

TIMI SCORE	NO OF PATIENTS
0-1	3
2	15
3	13
4	9
5	1

# **CORRELATION OF MHR WITH TIMI**

Since TIMI score was an ordinal variable and MHR was a continuous variable, spearman's correlation was carried out to assess the relationship between Monocyte HDL-c ratio and TIMI score.

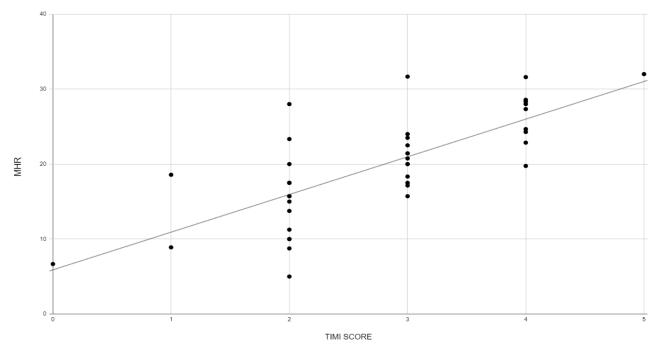


Fig.1: scatterplot of MHR and TIMI score along with trend line

The spearman's correlation coefficient (rho value) for MHR and TIMI was observed to be .746 with a significance value (2 tailed p) <0.0001. A high positive correlation was seen between MHR and TIMI scores.

It can be inferred that the MHR value is 74.6% in correlation with the TIMI score. Cut off value of the MHR for high TIMI score was calculated using the ROC curve. With a sensitivity of 90% and specificity of 86%, the cut-off value of MHR for 3 vessel blocks was set at 22.67. The AUC was .911.

#### **CORRELATION OF MHR WITH ANGIO**

Since the number of vascular occlusions was an ordinal variable and MHR was a continuous variable, spearman's correlation was carried out to assess the relationship between Monocyte HDL-c ratio and output of angiography.

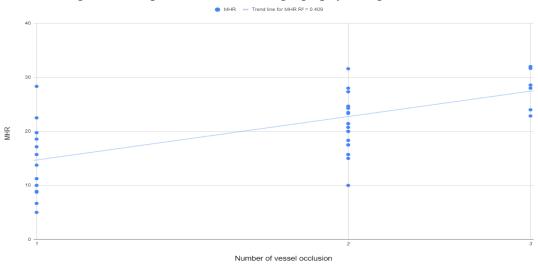


Fig.2: scatterplot of MHR and angiography along with trend line

The spearman's correlation coefficient (rho value) for MHR and angiography was observed to be .629 with a significance value (2 tailed p) < 0.0001. A moderate positive correlation was observed between

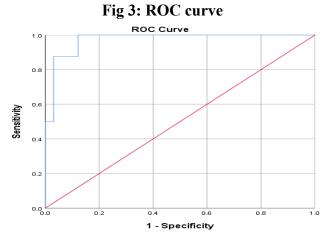
# MHR and angiography.

It can be inferred that the MHR value is 62.9% in correlation with Angiography

Cut off value of MHR for the 3 vessel blocks was calculated using the ROC curve. With sensitivity of 83.3% and specificity of 83% the cutoff value of MHR for 3 vessel blocks was set at 23.75. The AUC was .975.

#### MHR AS A PREDICTOR OF MACE IN HOSPITAL

Among the 41 study subjects, in hospital death occurred among 6 patients. An ROC curve analysis was done to determine the cut off value of the MHR ratio.



The area under the curve was highly significant with .973. At a cut off value of 23.75 the sensitivity and specificity of MHR for MACE were 87.5% and 88%.

The risk ratio for higher MHR(>23.75) for MACE was calculated as 9.54 with a 95% confidence interval of 2.32 to 39.15. This can be inferred as patients presenting with high monocyte to HDL ratio are almost ten times more likely to have another cardiac event which can increase the in-hospital mortality.

#### **DISCUSSION:**

The average age of the study samples in the present study was  $54.07 \pm 7.31$  years. The age of the study samples ranged from 36 years to 67 years. In the present study, the mean age among men was  $51.85 \pm 7.1$  years and the mean age among women was  $58.25 \pm 5.2$  years. In a similar study<sup>14</sup> based on the acute coronary syndrome in India, the mean age of presentation was observed to be  $56.06 \pm 11.29$  years. Among men, it was observed to be  $54.5 \pm 10.87$  years, whereas, among women, it was  $60.97 \pm 11.23$  years (P = .000). The findings of the present study in terms of the age of the study population can be compared with the aforementioned study.

Numerous premature Acute Coronary syndrome has been reported in many studies pertaining to India. <sup>15</sup> Most of the causes have been attributed to the prevalence of family history of Cardio Vascular Diseases, smoking, and hypertension. <sup>15</sup>

In the present study, the prevalence of smoking among the study population was 51% and when adjusted with sex the prevalence was found to be 77.77%. In a study based in India, the prevalence of smoking was 39%. <sup>15</sup>

In the current study, the prevalence of family history of coronary artery disease was 56%. In a case-control study<sup>16</sup>, the prevalence of family history among the cases was found to be 49%.

87% of the study population in the current study was hypertensive at the time of presentation. In GUSTO trial<sup>17</sup> it was established that 40% of the people who presented with the acute coronary syndrome were previously diagnosed hypertensive patients. The prevalence of hypertension among the Indian population is 13.8% in men and 8.8% in women.<sup>18</sup> With the increase in the trend of noncommunicable diseases, the disease burden pertaining to Acute Coronary Syndrome as time

progresses will be uncontrollable. Necessary interventions should be put forward in minimizing the risk factor exposures.

# Lipid profile

The mean HDL-c among the study subjects in the present study was  $35\pm 5$  mg/dl. The mean total cholesterol in the present study was  $360\pm 17$  mg/dl. The mean LDL level in the present study was 161 mg/dl. In a study based on Indonesia by Manurung et al <sup>19</sup> the mean HDL-c among 391 patients was 42.84 mg/dl +/- 10.28. The mean LDL cholesterol level was 36.16 mg/dl +/- 47.29. The mean value of total cholesterol level was 205.23 mg/dl +/- 54.84.In clinical research by Pitt et al <sup>20</sup>, the mean HDL value among the cases was 39.1 mg/dl, the mean Total cholesterol was 200 mg/dl and the mean LDL cholesterol level was 136 mg/dl. In a study based in Europe by Correia et al <sup>21</sup>, the mean HDL value among the cases was  $39\pm 10$  mg/dl, the mean Total cholesterol was  $199\pm 44$  mgl/dl and the mean LDL cholesterol level was  $128\pm 1.1$ . In a cross-sectional study for assessment of lipid level in Acute Coronary Syndrome by Fleischmann et al <sup>22</sup>, the mean HDL value among the cases was 39.1 mg/dl, the mean Total cholesterol was 230 mg/dl and the mean LDL cholesterol level was 136.2 mg/dl. Compared to the other studies, the lipid profile in the present study is different. The mean HDL of the present study is lower compared to other studies. The mean LDL is higher in the present study compared to other four studies.

#### **MONOCYTES and WBC.**

The total monocyte count was elevated in the majority of the study population in the present study. The average monocyte count among the study population was  $662\pm183$  cells/mm<sup>3</sup>. The average WBC count of the study population was  $11577\pm2351$  cells/mm<sup>3</sup>. The average neutrophil and lymphocyte count of the study population is  $5043\pm1173$  and  $5370\pm1153$  respectively.

In a sudy based on Saudi Arabia by Khan et al.,<sup>23</sup> it was observed that monocytes were significantly increased among patients with Acute Coronary Syndrome. The mean monocyte count in the study population was 793 cells/cumm. The average WBC count was 11500 cells/cumm.

In a study by Meisel S.R et al.,<sup>24</sup> it was observed that 58% of the study population with Acute Coronary Syndrome, had a monocyte count of more than 800/mm<sup>3</sup>. The mean monocyte count in the study was observed to be 800/mm<sup>3</sup>. In the present study, 26% of the study population had a monocyte count more than 800/mm<sup>3</sup>.

The monocyte count was significantly elevated among patients with Acute Coronary Syndrome in a study trying to establish the relationship between lymphocyte count. In the study conducted by Nunez et al.,<sup>25</sup> the mean monocyte count was 806/mm<sup>3</sup>. The study declared that monocyte count individuals cannot be considered as a predictor for future cardiac events.

#### **MHR**

The average MHR obtained among the study population was  $19.62 \pm 6.92$  in the present study. The range of MHR obtained was 5 - 32. 80% of the study population had an MHR ratio of more than or equal to 15.

In a study by Ganjali et al<sup>26</sup> the mean MHR ratio was 14.5. The odds ratio for high MHR in in-hospital mortality was found to be 3.10.

In a study with similar setting by Oylumlu et al.,<sup>27</sup> the mean MHR ratio of the patients with the acute coronary syndrome was calculated to be 18.5. A high MHR of more than 15 was correlate with inhospital mortality.

In the study by Karatas et al.<sup>28</sup>, the analysis showed MHR greater than 17.1 as a cutoff value for mortality and MHR greater than 20.4 as a cutoff value for MACE. the risk ratio of high MHR was calculated as 4.71. In the present study, the cut-off value for MACE/in-hospital mortality was calculated as 23.75 with a sensitivity of 87.5% and specificity of 88%. The risk ratio for high MHR was calculated as 9.54. In a study by Cicek et al.,<sup>29</sup> high MHR had a risk ratio of 10.60 which can be

compared to the present study.

# MHR TO TIMI CORRELATION

In a study by Sercelik et al.,  $^{30}$  a significant correlation was found between TIMI score and MHR. The correlation coefficient observed in the aforementioned study between TIMI and MHR was 0.479 with a p<0.0001. The cutoff value of MHR for high TIMI score in patients with STEMI was 2.409, with a sensitivity of 43.06% and a specificity of 87.18% (AUC 0.669; 95% CI 0.569-0.8769; p=0.003) on ROC curve analysis.

In the present study, the spearman's correlation coefficient (rho value) for MHR and TIMI was observed to be .746 with a significance value (2 tailed p) <0.0001. A high positive correlation was seen between MHR and TIMI scores. It can be inferred that the MHR value is 74.6% in correlation with the TIMI score. A cut-off value of the high TIMI score was calculated using the ROC curve. With a sensitivity of 90% and specificity of 86%, the cut-off value of MHR for 3 vessel blocks was set at 22.67. The AUC was .911.

#### **CONCLUSION:**

MHR is a new cost-effective, logical and good predictive marker for coronary vascular diseases. Multiple studies have emphasized the utilization and findings relating to MHR. MHR can be used as a good prognostic factor for the short term, among patients with Acute Coronary syndrome.

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