Reduced coronary blood flow can lead to cardiac ischemia and insufficient oxygen supply to the heart, which can cause Acute Myocardial Infarction (AMI) [1]. Numerous causes contribute to reduced coronary blood flow. Usually, atherosclerotic plaques burst and induce thrombosis, which causes a sudden drop in coronary blood flow [2]. Acute Myocardial Infarction (AMI), also referred to as heart attack, continues to be one of the world’s major causes of mortality and morbidity. A deep understanding of the underlying mechanism of the disease is necessary for enhancing an effective therapy, prompt identification and risk assessment for this life threatening illness. In the last few years, an increased interest is seen in the function of trace elements like copper [3]. Copper being an antioxidant element, is important for energy metabolism, formation of connective tissue formation and neurotransmitter. Its involvement in copper dysregulation, oxidative stress, inflammation and endothelial dysfunction has been implicated in several cardiovascular diseases including AMI [3]. The biochemical processes in the heart muscle that are vital to cardiac metabolism and function entail copper, an important micronutrient for human health and development. One of study found that dietary copper supplementation replenished heart copper, increased

**Objective:** To find the changes in serum copper level in patients with Acute Myocardial Infarction (AMI).

**Methods:** This observational study was conducted in District Headquarter Hospital, Nowshera in duration of two years. A total of 240 patients were recruited in this study. Upon admission, demographic information, medical history, and clinical characteristics were collected. Blood samples were obtained for measurement of serum copper levels using established laboratory methods. All data were analyzed through SPSS version 29.0.

**Results:** Among total, 65% males and 35% females and the prevalence of cardiovascular risk factors was notable, with 70% of patients having hypertension, 40% with diabetes mellitus, 60% with dyslipidemia, and 45% identified as smokers. Baseline serum copper levels averaged 110 ± 5.2 µg/dL, within 24 hours of admission, the peak serum copper level significantly increased to 125 ± 18.6 µg/dL. Subsequently, levels decreased gradually over the following days, with mean values of 120 ± 17.1 µg/dL on Day 2, 115 ± 16.4 µg/dL on Day 3, 112 ± 15.9 µg/dL on Day 4, and returning to baseline levels by Day 5, 110 ± 15.2 µg/dL.

**Conclusions:** Serum copper levels exhibit significant changes during the acute phase of AMI, with a peak observed within 24 hours of admission. While patients with anterior infractions showed higher peak copper levels, no significant associations were found between copper levels and traditional cardiovascular risk factors or inflammatory markers.
VEGF, promoted angiogenesis, and reversed mouse hypertrophic cardiomyopathy [4]. Although there is an increasing evidence pointing to a possible correlation between AMI and copper levels, the specifics of this correlation are yet not clear. Regarding variations in serum copper levels in patients with AMI, researches has given contradictory results; some have suggested high levels as a sign of oxidative stress, while others have suggested low levels as a result of acute myocardial damage [5]. Since Cardiovascular Disease (CVD) is the leading cause of morbidity and mortality globally, it is a serious threat to global public health. Despite current understanding, estimates suggest that by 2030, approximately 45% of adult Americans would have a (CVD). Globally, the top two causes of death and disability among individuals over 50 are ischemic heart disease and stroke[6]. While the known function of traditional risk factors in the pathophysiology of cardiovascular disease is well understood, new risk factors must be investigated in order to understand evolving mechanisms. Though findings are not consistent, there has been an increase in interest recently in the connection between CVD and metals like copper. Elevated exposure to certain metal compounds has fueled this interest, particularly regarding copper, which despite its vital role in cell metabolism, can also instigate oxidative stress through reactive oxygen species formation [7]. Serum copper levels serve as a valuable biomarker for assessing the body's copper status. The association between the Coronary Artery Disease (CAD) and trace elements shows two crucial aspects; one the protective role played to drinking water hardness due to the minerals including Chromium(Cr), magnesium(Mg), selenium(Si), and zinc(Zn) [8]. While the other minerals such as lead(Pb), manganese (Mn), and cadmium (Cd) are target to cause harmful to drinking water. Secondly, the involvement of serum level alteration of these trace elements following the ischemic heart disease and acute myocardial infarction [9]. The alteration has been dissimilar; for instance, stress inducing act such as marathon running have been found decrease significantly the level of serum Mg and Zn but not seen any change in Serum Cu level. Moreover, the previous experiments showed the association of coronary artery ligation in other animals like dogs have revealed marked decrease in level of serum Zn, while the level of Ca and Mg remained stable and unchanged[10]. The aim of this study was to investigate assessing baseline serum copper levels in patients treated for Acute Myocardial Infarction (AMI). Through an analysis of these baseline values, we looked at possible clinical consequences. Increased copper levels might be used as a biomarker to guide therapies and lifestyle changes related to cardiovascular risk assessment.

M E T H O D S
This prospective observational study was conducted in District Headquarter Hospital, Nowshera, Khyber Pakhtunkhwa in duration of two years November 2021 to November 2023. The study included 240 patients, estimated using WHO software for sample size estimation. The sample size was based on a 20.8% percentage of AMI, a 95% confidence interval, and a 5% margin of error. The sample approach used was non-probability consecutive sampling. Patients aged ≥18 years, diagnosis of AMI based on clinical symptoms, electrocardiographic changes, and elevated cardiac biomarkers (troponin, CK-MB) were included in the study. While history of prior myocardial infarction or coronary revascularization, active malignancy, chronic inflammatory diseases, or other conditions affecting copper metabolism, and pregnancy or lactation were excluded from the study. The study was approved by Institution Review Board(IRB) on dated: 14-10-2021 with Reference No: ERB/DHQ/21/04. Upon admission, demographic information, medical history, and clinical characteristics of eligible patients were collected using standardized case report forms. Blood samples were obtained for measurement of serum copper levels using established laboratory methods. Serial blood samples were collected at predefined intervals during hospitalization and at follow-up visits for assessment of dynamic changes in copper levels over time. Patients underwent comprehensive clinical evaluation, including assessment of cardiovascular risk factors (hypertension, diabetes, dyslipidemia, smoking), comorbidities, and medication history. Cardiac imaging studies were performed as clinically indicated to evaluate myocardial function and coronary artery anatomy. Data were analyzed using SPSS version 29.0. Descriptive statistics were used to calculate and summarize the demographic and other clinical features of the studied participants/patients. Changes in serum copper levels over time were analyzed. Pearson correlation coefficient were used for p-value determination between serum copper levels and inflammatory markers. All data presented in the tables. P-value less than <0.05 were considered significant.

R E S U L T S
Data were collected from 240 patients. Mean age was 62.5 ± 8.3 years. There were 65% males and 35% females and the prevalence of cardiovascular risk factors was notable, with 70% of patients having hypertension, 40% with diabetes mellitus, 60% with dyslipidemia, and 45% identified as smokers. Baseline serum copper levels averaged 110 ± 15.2 μg/, indicating a varied range of copper concentrations within the study population(Table 1).
During the acute phase of Acute Myocardial Infarction (AMI), dynamic changes were observed in serum copper levels. At baseline, the mean serum copper level was 110 µg/dL with a standard deviation of 15.2. Within 24 hours of admission, the peak serum copper level significantly increased to 125 µg/dL (± 18.6). Subsequently, levels decreased gradually over the following days, with mean values of 120 µg/dL (± 17.1) on Day 2, 115 µg/dL (± 16.4) on Day 3, 112 µg/dL (± 15.9) on Day 4, and returning to baseline levels by Day 5 (110 µg/dL ± 15.2) (Table 2).

Table 2: Changes in Serum Copper Levels

<table>
<thead>
<tr>
<th>Time Points</th>
<th>Serum Copper (µg/dL) (Mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>110 ± 15.2</td>
</tr>
<tr>
<td>Peak (within 24 hours)</td>
<td>125 ± 18.6</td>
</tr>
<tr>
<td>Day 2</td>
<td>120 ± 17.1</td>
</tr>
<tr>
<td>Day 3</td>
<td>115 ± 16.4</td>
</tr>
<tr>
<td>Day 4</td>
<td>112 ± 15.9</td>
</tr>
<tr>
<td>Day 5</td>
<td>110 ± 15.2</td>
</tr>
</tbody>
</table>

Peak troponin levels exhibited a strong positive correlation with serum copper levels ($r = 0.45$, $p < 0.001$), indicating a potential link between copper metabolism and myocardial damage. Similarly, peak CK-MB levels demonstrated a significant positive correlation with serum copper levels ($r = 0.38$, $p < 0.001$), further supporting the notion of copper's involvement in AMI pathogenesis. However, no significant correlations were found between serum copper levels and inflammatory markers, including CRP levels ($r = 0.12$, $p = 0.15$) and interleukin-6 levels ($r = 0.08$, $p = 0.32$) through Pearson correlation coefficient (Table 3).

Table 3: Association of Biomarkers in AMI Patients with serum copper levels

<table>
<thead>
<tr>
<th>Variables</th>
<th>Serum copper Correlation Coefficient ($r$)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak Troponin Levels</td>
<td>0.45</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak CK-MB Levels</td>
<td>0.38</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CRP Levels</td>
<td>0.12</td>
<td>0.15</td>
</tr>
<tr>
<td>Interleukin-6 Levels</td>
<td>0.08</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Heart failure was the most common complication, occurring in 20% of patients, followed by arrhythmias in 15% and cardiogenic shock in 8%. Additionally, a subset of patients experienced other complications, collectively accounting for 5% of cases (Table 4).

Table 4: In-Hospital Complications in AMI Patients

<table>
<thead>
<tr>
<th>Complications</th>
<th>Percentage of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Failure</td>
<td>20</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>15</td>
</tr>
<tr>
<td>Cardiogenic Shock</td>
<td>8</td>
</tr>
<tr>
<td>Others</td>
<td>5</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Our study reveals dynamic changes in serum copper levels during the acute phase of AMI, with a mean peak level of 125 µg/dL observed within 24 hours of admission, followed by a gradual decline to baseline levels over subsequent days. This study suggests strong association between alterations in the copper metabolism and AMI, possibly reflecting the release of copper from damaged myocardial tissue or changes in copper-binding proteins in response to oxidative stress and inflammation [10]. Interestingly, subgroup analysis demonstrates that patients with anterior myocardial infarction exhibit higher peak copper levels compared to those with inferior or lateral infarctions [11]. The most notable change observed in this study was the lower level of serum copper leads towards the acute myocardial infarction, particularly noteworthy among the trace divalent cations evaluated. Notably, this reduction did not reach statistical significance in females, likely due to their limited representation in the sample [12]. Nonetheless, we propose that such a reduction in serum copper levels could serve as a potential diagnostic marker for acute myocardial infarction [13]. While it is imperative to rule out causes of hypocupremia including the advance syndrome of malabsorption and the Wilson's disease, these conditions are either clinically apparent or rare occurrences [14]. The copper level in serum are increasing without treatment 125 ± 18.6 µg/dL observed in 1st 24 hours in Acute Myocardial Infarction (AMI) patients in our study but according to Omar M. Hameed in 2023 The level of Cu was observed to be significantly (P<0.05) higher in the serum of control people (118.50 ± 12.04 µg/dL) but according to S Begum et al 2023 control and case group respectively the copper was 105.44 ± 24.15µg/dL and 146.49 ± 23.52µg/dL [10, 15]. Asian persons had higher serum Cu levels than healthy controls SMD = 2.191, 95% CI = [1.401, 2.981] Z = 5.43, p < 0.001) whereas Caucasian individuals did not have higher serum Cu levels than MI SMD = 0.411, 95% CI = [−0.030, 0.861] Z = 1.83, p = 0.068). Increased serum Cu levels and MI are strongly correlated [16]. Serum Cu levels were significantly lower in the acute coronary syndrome group compared to the control group (p<0.001). Aysegül Bayir et al., in 2013, reported that there was a significant
difference in serum Cu levels between patients with ACS and healthy control persons [17]. Increased risk factors for myocardial infarction total stroke and cardiovascular mortality have been associated with elevated levels of S-Cu. It indicates that hybrid research has changed the degree of association between S-Cu and the risk of ischemic stroke and cardiovascular mortality [18]. There is a strong association between serum trace element concentrations and certain coronary risk factors [19]. It was discovered that serum Cu and MT levels had considerably risen. The blood Zn and Cu levels in the subgroup of individuals who died were considerably lower [20]. The prevalence of cardiovascular risk factors was 65% in male and 35% females in our study is compare with Andersen et al., which reported that 47.9% females and 52.1% males with cardiovascular risk [21] but according to Wang et al., 2020 the higher prevalence in female then the male which is n=15,490 (39.4%) male and n=23,769 (60.5%) females patient which Acute Myocardial Infarction (AMI) large population Cohort study conducted by China [22]. Taghavi et al., 2020 shows that highest number of cardiac patients was male (65%) and female were 35% with the mean serum copper was 189.28 ± 58.3 [23]. Our study finding shows 8% of Acute Myocardial Infarction (AMI) patients have Cardiogenic shock is compared with Bertaina M et al., in 2023 the 80% of Cardiogenic shock in Acute Myocardial Infarction (AMI) patents and 15% of of Acute Myocardial Infarction (AMI) patients were Arrhythmias[24] but according to Al Khatib et al., in 2023. However it was also reported that during the peri-infarction phase, arrhythmias occur in around 75% of individuals with Acute Myocardial Infarction (AMI) [25]. Heart failure, which affects 20% of patients after an Acute Myocardial Infarction (AMI), is the most prevalent consequence, followed by arrhythmias in 15% of cases and cardiogenic shock in 8% of cases when compared across studies. In addition, 5% of cases were caused by various problems combined [26, 27]. A different study found that in-hospital mortality was 59.5% and that mechanical complications, including cardiac arrest, cardiac septal dissection, and Mitral Regurgitation (MR), were seen in 3.5 out of every thousand cases with AMI [28]. In addition, patients with Cardiogenic Shock linked to Heart Failure (HF-CS) had a reduced in-hospital mortality rate, a lower age, and a lower number of cardiac arrests in contrast to patients with cardiogenic shock due to AMI [29]. When considering several forms of cardiogenic shock in the setting of an acute myocardial infarction, these results highlight the differences in their clinical presentations and results.

**Conclusions**

This study concludes that during the acute phase of AMI, a significant change in serum copper levels are seen, peaking within 24 hours of admission. Although patients with anterior infarcts had high copper levels, no meaningful associations were seen between levels of copper and inflammatory markers or cardiovascular risk factors.

**Authors Contribution**

Conceptualization: SAO
Methodology: SAO, PM
Formal analysis: PM, AK
Writing, review and editing: MK, FAB, HUR

All authors have read and agreed to the published version of the manuscript.

**Conflicts of Interest**

The authors declare no conflict of interest.

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**References**


