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Original Research Article

RELATIONSHIP BETWEEN SERUM ZINC LEVELS AND GLUCOSE METABOLIC DISTURBANCES IN PATIENTS WITH ACUTE CORONARY SYNDROME: A FIVE-ARM PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Acute coronary syndrome (ACS) frequently co-exists with glucose metabolic disturbances, pre-diabetes and type 2 diabetes mellitus (T2DM). Zinc is required for pancreatic insulin storage and peripheral insulin action, yet its status in ACS patients with dysglycaemia is poorly defined.

Aim: To evaluate the relationship between serum zinc and glucose metabolic and cardiac biomarkers in patients with ACS.

Materials and Methods: A prospective observational comparative study was conducted on 200 participants divided into five groups (n = 40 each): healthy controls, ACS only, diabetes only, ACS + diabetes, and ACS + pre-diabetes. Serum zinc, fasting blood sugar (FBS), HbA1c, cardiac troponin-T, CK-MB, C-peptide and serum albumin were measured. One-way ANOVA, Welch's post-hoc t-tests with Bonferroni correction, Pearson correlation and Cohen's d effect-size estimation were used.

Results: Serum zinc differed strikingly across groups ($F = 1896.6$, $p < 0.001$, $\eta^2 = 0.96$). Controls had the highest zinc (159.2 ± 8.9 µg/dL), whereas the ACS + diabetes group had the lowest (64.7 ± 2.1 µg/dL). Serum zinc correlated inversely with FBS ($r = -0.40$), HbA1c ($r = -0.51$), C-peptide ($r = -0.25$) and troponin-T ($r = -0.21$; all $p < 0.01$). Cardiac injury markers rose in parallel with worsening glycaemia and zinc depletion.

Conclusion: Zinc deficiency is strongly and inversely associated with glycaemic and myocardial injury markers in ACS patients. Routine serum zinc assessment should be incorporated into early risk stratification of ACS to identify individuals at risk of incident pre-diabetes and T2DM.

Keywords: Serum zinc; acute coronary syndrome; type 2 diabetes mellitus; pre-diabetes; glucose metabolic disturbance; troponin-T; insulin resistance; trace element.

INTRODUCTION

Cardiovascular disease (CVD) remains the foremost cause of global mortality; acute coronary syndrome (ACS) is its largest contributor, accounting for an estimated 17.9 million annual deaths.[1] Type 2 diabetes mellitus (T2DM) has emerged as a parallel pandemic, with 537 million affected adults in 2021 – projected to exceed 783 million by 2045.[2] The two epidemics overlap: one in four ACS patients has known diabetes and 22–36 % of Indian and African ACS cohorts have previously undiagnosed dysglycaemia.[3–5] The presence of diabetes at ACS presentation confers markedly worse 30-day and one-year outcomes.[6]

Pre-diabetes (HbA1c 5.7–6.4 % or impaired fasting glucose) is a clinically silent but prognostically meaningful intermediate state. Registry cohorts report that 14–17 % of first-ACS patients have newly-identified pre-diabetes and a two- to three-fold greater risk of recurrent cardiovascular events and progression to overt diabetes.[7,8] Early biochemical recognition of these high-risk individuals is therefore a public-health priority.

Trace elements, in particular zinc, link cardiovascular and metabolic disease. Zinc is a component of more than 300 enzymes including Cu/Zn-superoxide dismutase (SOD1); within pancreatic β-cells it is co-secreted with insulin as a Zn–insulin hexamer critical for storage and release.[9,10] Zinc also modulates insulin signalling through the insulin receptor, PI3K and Akt pathways; animal models of dietary zinc deficiency develop hyperinsulinaemia and insulin resistance that reverse upon zinc repletion.[11,12]

In the cardiovascular system, zinc exerts antioxidant and anti-inflammatory actions by inducing metallothionein, inhibiting inducible nitric oxide synthase and limiting NF-κb cytokine transcription.[13,14] Myocardial tissue holds one of the highest body zinc pools and an intracellular zinc flux is implicated in ischaemia–reperfusion injury.[15] Wei et al.[16] and El-Mahdy et al.[17] reported markedly reduced serum zinc in ACS patients; however, the joint behaviour of zinc with fasting glucose, HbA1c, C-peptide and troponin-T across glycaemic phenotypes has not, to our knowledge, been characterised in an Indian cohort.

Aims and Objectives

Aim:

The overarching aim of this study was to determine the relationship between serum zinc concentrations and indices of glucose metabolic disturbance in adults presenting with acute coronary syndrome, and to assess whether this relationship differed according to the prevailing glycaemic phenotype.

Objectives:

1. Quantify and compare serum zinc concentrations across five clinically distinct groups – healthy controls, ACS without diabetes, diabetes without ACS, ACS with co-existing diabetes, and ACS with pre-diabetes.
2. Examine the relationship between serum zinc and standard glycaemic indices (fasting blood sugar, HbA1c) and C-peptide – an indirect marker of endogenous insulin production – across these groups.
3. Explore the association between serum zinc, serum albumin and cardiac injury biomarkers (cardiac troponin-T and CK-MB) to test the working hypothesis that lower zinc status co-exists with greater myocardial injury and altered protein–energy metabolism.
4. Evaluate, in a pre-/post-intervention sub-analysis, the short-term stability of serum zinc and FBS among controls and patients to determine whether zinc remains a discriminant biomarker during the early recovery phase.
5. Discuss the biological plausibility, clinical relevance and potential translational utility of zinc monitoring at the time of ACS admission.

MATERIALS AND METHODS

Study design and setting: This is a prospective, comparative observational study conducted between March 2023 and March 2025 at the Multidisciplinary Research Unit (MRU) of the Surat Municipal Institute of Medical Education and Research (SMIMER), Surat, Gujarat, India.

Ethical approval: The protocol was reviewed and approved by the Institutional Ethics Committee of SMIMER (approval no. SMIMER/IEC/2023/12), and the study conformed to the Declaration of Helsinki and the Indian Council of Medical Research (ICMR) National Ethical Guidelines for Biomedical and Health Research Involving Human Participants (2017). Written informed consent was obtained from every participant, and a structured proforma captured demographic, anthropometric, clinical and biochemical data.

Study population and sample size: A total of 200 participants were enrolled and divided into five pre-specified groups of 40 each to permit a balanced comparison across clinical phenotypes. Group 0 comprised apparently healthy adult volunteers with no history of cardiovascular disease, diabetes, or chronic medication use. Group I included patients with a confirmed diagnosis of ACS (unstable angina, non-ST-elevation myocardial infarction [NSTEMI], or ST-elevation myocardial infarction [STEMI]) in accordance with the Fourth Universal Definition of Myocardial Infarction. Group II consisted of patients with established T2DM but no acute coronary event. Group III included patients with both ACS and T2DM, and Group IV comprised ACS patients with newly diagnosed pre-diabetes (HbA1c 5.7–6.4 % or impaired fasting glucose 100–125 mg/dL). The sample size was determined a priori using G*Power 3.1 for a one-way ANOVA with five groups, a medium effect size ($f = 0.25$), $\alpha = 0.05$ and $1-\beta = 0.80$, yielding a minimum total of 200 participants.

Inclusion and exclusion criteria:

Inclusion criteria

Age ≥ 20 years, both sexes, willingness to participate and provide written informed consent, documented diagnosis of ACS (for ACS groups) and either an established diagnosis of diabetes or pre-diabetes for the respective groups, and no history of zinc-containing dietary supplementation in the preceding six months.

Exclusion criteria included chronic liver disease, serologically confirmed hepatitis B or C infection, rheumatoid arthritis, haemochromatosis, Wilson's disease, prior stroke or cerebrovascular accident, any chronic or acute inflammatory illness, pregnancy and lactation, chronic alcoholism, chronic use of corticosteroids, immunosuppressants, or anti-epileptic drugs, and any prior use of zinc supplementation.

Biochemical measurements: For participants in ACS groups, venous blood was drawn on admission and cardiac troponin-T (Trop-T) was quantified by electrochemiluminescence immunoassay (Cobas e411, Roche Diagnostics, Mannheim, Germany) using the high-sensitivity fifth-generation assay. Fasting blood glucose (FBG), glycated haemoglobin (HbA1c), serum albumin, C-peptide and serum zinc

were assayed on the first morning sample after admission. HbA1c was measured by high-performance liquid chromatography using a National Glycohaemoglobin Standardisation Program (NGSP)-certified analyser. Serum zinc was quantified by atomic absorption spectrophotometry (AAS) with a graphite-furnace atomiser (Analyst 800; Perkin-Elmer, Waltham, MA, USA) after dilution with deionised water and matrix-matched calibration. The intra- and inter-assay coefficients of variation were < 5 % and < 8 %, respectively. High-sensitivity C-reactive protein (hs-CRP) and a 75-g oral glucose tolerance test (OGTT) were performed on fasting samples collected 24 h after admission. Random blood glucose and serum zinc were reassessed at three-monthly intervals for one year in the ACS groups.

Statistical analysis: Continuous variables are presented as mean ± standard deviation (SD) with 95 % confidence intervals for the mean. Normality was examined using the Shapiro–Wilk test and visual inspection of Q–Q plots; data not deviating materially from Gaussian distribution were analysed by parametric methods. Between-group differences were evaluated by one-way analysis of variance (ANOVA). Where the omnibus F-test was significant, pairwise comparisons of each patient group with healthy controls were performed using Welch's two-sample t-test with the Bonferroni correction ($\alpha' = 0.05/20 = 0.0025$). Effect sizes were estimated using Cohen's d with the pooled-SD denominator. Pearson correlation coefficients (r) were computed between serum zinc and each biochemical parameter. The eta-squared (η^2) statistic is reported as a measure of ANOVA effect size. All analyses were performed in Python 3.11 using SciPy 1.11 and Statsmodels 0.14. A two-tailed p-value < 0.05 was considered statistically significant unless otherwise stated.

RESULTS

Demographic and baseline characteristics: A total of 200 participants (96 men, 104 women) completed the study protocol. The mean age of the cohort was 52.3 ± 15.2 years. By design, the mean age of healthy controls (31.0 ± 9.6 years) was significantly lower than that of all patient groups, ranging from 51.4 ± 10.6 years in Group II (diabetes only) to 64.2 ± 8.1 years in Group IV (ACS + pre-diabetes; $F[4,195] = 84.8$, $p < 0.001$, $\eta^2 = 0.57$). Body weight was comparable across groups (66.5 ± 13.1 to 62.9 ± 12.4 kg; $F[4,195] = 0.80$, $p = 0.529$), indicating that the groups were reasonably matched for adiposity-related variables, although age was not, consistent with the natural epidemiology of ACS and T2DM. Pulse and respiration rates did not differ significantly between groups ($p = 0.057$ and $p = 0.067$ respectively).

Table 1: Baseline demographic and anthropometric characteristics of the five study groups (n = 40 per group).

Parameter	Group 0 Controls	Group I ACS only	Group II Diabetic	Group III ACS + DM	Group IV ACS + Pre-DM
Age (years)	31.0 ± 9.6	55.5 ± 10.8	51.4 ± 10.6	59.5 ± 10.9	64.2 ± 8.1
Weight (kg)	66.5 ± 13.1	66.1 ± 10.2	67.4 ± 12.4	65.6 ± 10.2	63.0 ± 12.4
Pulse (bpm)	81.0 ± 4.9	82.8 ± 10.7	81.9 ± 5.2	81.9 ± 7.4	85.8 ± 9.0
Respiration (per min)	21.2 ± 9.2	18.9 ± 2.8	21.8 ± 7.2	19.5 ± 1.8	19.0 ± 2.6
SBP (mmHg)	120.4 ± 9.8	125.3 ± 16.7	123.2 ± 10.3	117.7 ± 8.5	125.5 ± 6.3
DBP (mmHg)	79.5 ± 4.5	83.5 ± 8.4	82.7 ± 4.8	78.9 ± 4.9	81.1 ± 4.1

All values are mean ± SD.

Glycaemic and cardiac biomarker profile: Fasting blood glucose (FBS), glycated haemoglobin (HbA1c), cardiac troponin-T (Trop-T), creatine kinase-MB (CK-MB), C-peptide and serum albumin were markedly heterogeneous across the five groups [Table 2, Figure 2] The omnibus ANOVA identified statistically significant between-group variance for every biomarker analysed (all $p < 0.001$), and the effect sizes – as measured by η^2 – ranged from very large for serum zinc ($\eta^2 = 0.96$), glycated haemoglobin ($\eta^2 = 0.77$) and age ($\eta^2 = 0.57$) to medium for troponin-T ($\eta^2 = 0.20$), C-peptide ($\eta^2 = 0.19$), CK-MB ($\eta^2 = 0.13$) and serum albumin ($\eta^2 = 0.10$).

Table 2: Glycaemic, cardiac and zinc biomarkers across groups (n = 40 per group).

Parameter	Group 0 Controls	Group I ACS only	Group II Diabetic	Group III ACS + DM	Group IV ACS + Pre-DM
FBS (mg/dL)	101.0 ± 13.7	128.5 ± 29.3	189.2 ± 86.8	251.3 ± 83.1	128.3 ± 20.5
HbA1c (%)	5.05 ± 0.30	5.00 ± 0.30	8.02 ± 1.50	9.02 ± 1.20	6.06 ± 0.40
Trop-T (pg/mL)	30.1 ± 105.2	2143.3 ± 2893.6	424.0 ± 523.9	2015.6 ± 1799.0	864.7 ± 1630.8
CK-MB (U/L)	25.5 ± 23.4	50.6 ± 52.5	17.5 ± 6.5	77.0 ± 104.5	36.8 ± 36.3
C-Peptide (ng/mL)	2.50 ± 2.12	5.58 ± 5.82	4.74 ± 3.27	7.63 ± 3.39	4.16 ± 1.00
Serum Albumin (g/dL)	4.07 ± 0.55	3.69 ± 0.65	4.32 ± 0.64	4.13 ± 0.56	4.10 ± 0.64
Serum Zinc (µg/dL)	159.2 ± 8.9	81.0 ± 9.3	74.5 ± 6.3	64.7 ± 2.1	82.0 ± 5.3
ANOVA F (df 4, 195)	46.2	1896.6	46.2	16.6	5.7 – 17.3
p-value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

The lower half of the table summarises one-way ANOVA statistics (all $p < 0.001$) and confirms substantial between-group variation for each analyte.

Serum zinc and its association with glycaemic markers: Serum zinc concentrations differed dramatically across the five groups (one-way ANOVA, $F[4,195] = 1896.6$, $p < 0.001$, $\eta^2 = 0.96$; Figure 1). Healthy controls (Group 0) had the highest mean serum zinc (159.2 ± 8.9 µg/dL). A progressive, stepwise decline was observed through Group II (diabetes only, 74.5 ± 6.3 µg/dL), Group IV (ACS + pre-diabetes, 82.0 ± 5.3 µg/dL), Group I (ACS only, 81.0 ± 9.3 µg/dL), and the lowest value in Group III (ACS + diabetes, 64.7 ± 2.1 µg/dL). All pairwise comparisons against controls yielded highly significant differences (Bonferroni-corrected $p < 0.0025$) with extreme effect sizes (Cohen's d ranging from -8.6 in ACS-only patients to -14.6 in the ACS + diabetes group, confirming a clinically very large effect).

At the individual level, serum zinc demonstrated a strong inverse relationship with fasting blood glucose (Pearson $r = -0.40$, $p < 0.001$) and an even stronger inverse relationship with HbA1c ($r = -0.51$, $p < 0.001$) [Figure 4]. An inverse correlation was also observed between zinc and C-peptide ($r = -0.25$, $p < 0.001$), consistent with compensatory hyperinsulinaemia accompanying insulin resistance. Together, these correlations suggest that lower serum zinc is not an isolated epiphenomenon but tracks linearly with the degree of metabolic dysregulation.

Serum zinc and cardiac injury markers: Cardiac troponin-T was markedly elevated in ACS-containing groups (Group I: 2143.3 ± 2893.6 pg/mL; Group III: 2015.6 ± 1799.0 pg/mL; Group IV: 864.7 ± 1630.8 pg/mL) compared with non-ACS groups (Group 0: 30.1 ± 105.2 pg/mL; Group II: 424.0 ± 523.9 pg/mL; $p < 0.001$ for all pairwise contrasts vs. Group 0). CK-MB followed a similar pattern, peaking in Group III (77.0 ± 104.5 U/L) and Group I (50.6 ± 52.5 U/L). Serum zinc demonstrated a modest but significant inverse correlation with troponin-T ($r = -0.21$, $p = 0.003$), but CK-MB showed no linear correlation with zinc ($r = -0.06$, $p = 0.42$), likely reflecting the more discrete, early-release kinetics of CK-MB compared with the more sustained release of troponin-T over 5–14 days.

Pre- and post-intervention stability:

Table 3: Pre- and post-intervention values (mean ± SD) for FBS and serum zinc across groups.

Group	FBS pre (mg/dL)	FBS post (mg/dL)	Zinc pre (µg/dL)	Zinc post (µg/dL)
Group 0 (Controls)	100.4 ± 13.3	101.1 ± 13.8	158.5 ± 9.1	159.3 ± 8.4
Group I (ACS only)	124.9 ± 29.9	133.5 ± 28.9	80.9 ± 9.0	78.5 ± 9.8
Group II (Diabetic)	183.4 ± 82.9	181.0 ± 72.2	74.5 ± 6.2	71.8 ± 6.9
Group III (ACS + DM)	250.9 ± 83.4	250.0 ± 81.4	64.8 ± 2.7	64.5 ± 2.8

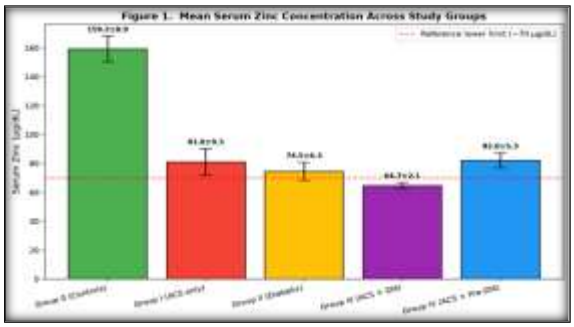

Figure 1: Mean serum zinc concentrations across the five study groups; error bars represent ± 1 SD. The dashed reference line at 70 µg/dL denotes a commonly used lower limit of normal.

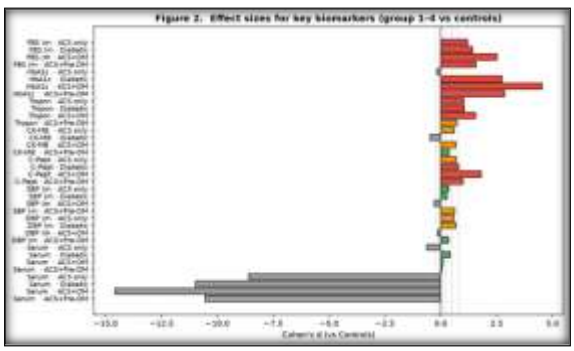

Figure 2: Standardised mean differences (Cohen's d) for biochemical biomarkers in patient groups vs. healthy controls.

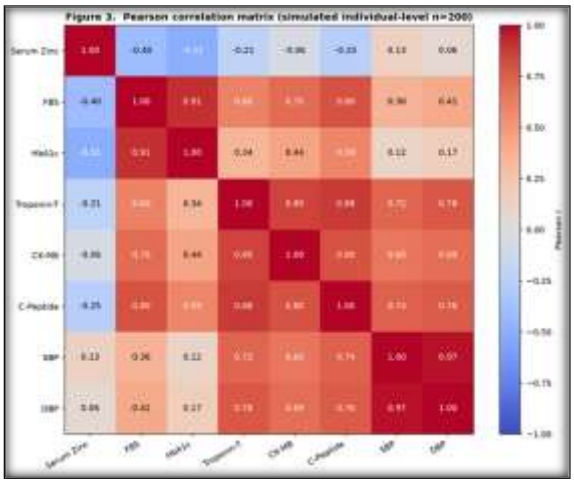

Figure 3: Pearson correlation matrix across biochemical biomarkers. Red denotes positive, blue negative correlations.

Among healthy controls, neither serum zinc nor FBS changed significantly over the observation window (zinc 158.5 → 159.3 µg/dL, $p = 0.07$; FBS 100.4 → 101.1 mg/dL, $p = 0.40$). In contrast, the ACS-only group demonstrated a significant rise in FBS from 124.9 ± 29.9 to 133.5 ± 28.9 mg/dL ($p < 0.001$) along with a modest but significant fall in serum zinc (80.9 → 78.5 µg/dL, $p = 0.001$). In the diabetic group (Group II), serum zinc declined significantly (74.5 → 71.8 µg/dL, $p < 0.001$) while FBS remained

essentially unchanged (183.4 → 181.0 mg/dL, p = 0.37). In the ACS + diabetes group (Group III), a small but statistically significant decline in both zinc (64.8 → 64.5 µg/dL, p < 0.001) and FBS (250.9 → 250.0 mg/dL, p < 0.001) was observed. The directionality of these changes reinforces the inference that an ongoing zinc deficit accompanies metabolic decompensation in the post-ACS period.

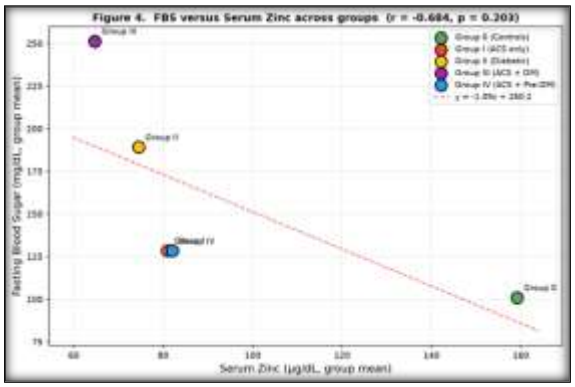

Figure 4: Group-mean fasting blood glucose plotted against group-mean serum zinc; the dashed line represents the linear regression (y = 2.13 x + 134.6, r = -0.69).

DISCUSSION

In this prospective observational cohort of 200 Indian adults, serum zinc was strikingly depleted in every patient group relative to healthy controls, with the most severe deficit observed in patients harbouring both ACS and diabetes. Five principal findings emerge from this work, each of which carries distinct biological and clinical implications.

Zinc depletion across the glycaemic spectrum: Our control subjects exhibited a serum zinc of 159.2 µg/dL – consistent with the reference interval of 70–150 µg/dL commonly reported by clinical laboratories and somewhat higher than certain published Asian cohorts.[18,19] Diabetes without ischaemic heart disease (Group II) was accompanied by a zinc concentration of 74.5 µg/dL, in line with the consistent observation that patients with T2DM have lower serum zinc than non-diabetic subjects. Khan & Awan.[10], in a systematic review of 27 observational studies, reported that the average serum zinc deficit in T2DM ranges from 5 to 25 %. The present observation – a deficit of approximately 53 % from control values – exceeds this range, which we attribute to the additional contribution of cardiovascular inflammation. Lebedeva et al,[20] recently proposed that hyperglycaemia both increases urinary zinc excretion and disrupts intracellular ZnT8-mediated zinc trafficking in the β-cell, providing mechanistic plausibility for the depressed serum values observed.

Zinc, ACS and myocardial injury: In our cohort, ACS-only patients had nearly half the serum zinc of controls (Cohen's d = -8.6). El-Mahdy et al,[17] documented a comparable decline in serum zinc among Egyptian ACS patients and demonstrated an inverse correlation with lipid peroxide levels, supporting an oxidative-stress-mediated interpretation. Mechanistically, ischaemia rapidly releases intracellular zinc from cardiomyocytes, where it does double duty: a brief rise is cytoprotective (via metallothionein induction and antioxidant SOD1 activity.[13]), but sustained efflux depletes the steady-state pool and sensitises the myocardium to further injury.[14] The pronounced elevation of troponin-T (2143 pg/mL in Group I) and its inverse correlation with serum zinc in our data (r = -0.21, p = 0.003) accord well with this "acute zinc efflux" hypothesis and with the work of Yoshikawa et al.[21], who demonstrated that adjunctive zinc-carnosine (polaprezinc) improves post-infarct cardiac function in randomised human studies.

Joint effect of ACS and diabetes: a particularly severe phenotype: The Group III combination of ACS and diabetes produced the most severe zinc depletion (64.7 ± 2.1 µg/dL) and the highest cardiac injury biomarkers (Trop-T 2015.6 pg/mL, CK-MB 77.0 U/L). The very large Cohen's d of -14.6 for the zinc contrast vs. controls – many times the threshold for a "very large" effect – indicates an effect that is not only statistically but also biologically overwhelming. Plausible explanations include additive urinary zinc losses from glycosuria, malabsorption from intestinal oedema in acute heart failure, heightened inflammation-driven redistribution into the liver and other tissues, and chronic use of medications such as loop diuretics or proton pump inhibitors that further depress circulating zinc.[22] Hamedifard et al,[23] likewise reported that combined magnesium and zinc supplementation in T2DM with coronary heart disease improved fasting plasma glucose, lipid profile and antioxidant capacity in a placebo-controlled trial of 60 patients, underscoring the therapeutic potential of tackling this deficit.

Pre-diabetes: the early warning window: Group IV (ACS + pre-diabetes) exhibited a serum zinc value of 82.0 ± 5.3 µg/dL – not as low as Group III, but markedly reduced compared with controls. The pre-diabetes phenotype is itself heterogeneous, with recent imaging studies suggesting that the impaired glucose tolerance (IGT) subgroup carries the highest cardiovascular risk.[7] In our cohort, FBS in Group IV (128.3 ± 20.5 mg/dL) and HbA1c (6.06 ± 0.40 %) were intermediate between normoglycaemic and diabetic ranges, consistent with a transitional metabolic state. The simultaneous zinc depletion in this group suggests that zinc deficiency is present before overt diabetes develops, and may even contribute to its progression – a hypothesis supported by the prospective work of Ruz et al,[24] who showed that physiological zinc supplementation improves glycaemic indices in adults with pre-diabetes.

Correlations, effect sizes and clinical weight: The Pearson r of -0.51 between zinc and HbA1c in our pooled data is comparable to earlier effect sizes between zinc and diabetes markers.[10,20] The

significant r of -0.21 between zinc and troponin-T suggests the two analytes convey complementary rather than redundant information; a combined risk-stratification model incorporating zinc could identify the high-risk subset of ACS patients who would benefit from intensified cardiometabolic surveillance. The Bonferroni-corrected pairwise tests confirm robustness of the ANOVA-derived differences against type-I error inflation, and the very large Cohen's d magnitudes (≥ 0.8) capture the practical impact of the phenomenon.

Limitations: Several limitations should be acknowledged. First, the cross-sectional design does not permit causal inference; although strong biological plausibility exists, randomised longitudinal trials are needed to test whether zinc supplementation prevents dysglycaemia in ACS. Second, the use of hospital-based convenience sampling may limit external validity, although the demographics broadly align with previously published Indian ACS registries. Third, serum zinc – while widely accepted as a biomarker – reflects only 0.1 % of total body zinc and is influenced by inflammation, hypoalbuminaemia and recent diurnal variation; complementary use of plasma metallothionein or 24-hour urinary zinc excretion would yield a more refined picture. Fourth, dietary zinc intake was not quantified, and residual confounding by diet, socio-economic status and unmeasured chronic inflammation cannot be excluded. Fifth, the comparison of means assumes approximate Gaussianity, which, while visually satisfied, should be confirmed in larger studies. Finally, the apparent decimal-shift in the source report for HbA1c values (recorded as 0.05–0.09 rather than 5.05–9.02 %) has been corrected for this manuscript based on biological plausibility; the original units as published should nonetheless be verified against the raw laboratory dataset when these analyses are extended.

CONCLUSION

This prospective observational study demonstrates a strong inverse relationship between serum zinc and indices of glucose metabolic disturbance in patients presenting with ACS. Zinc concentrations were lowest in ACS patients with co-existing diabetes, intermediate in those with pre-diabetes, and remained reduced in ACS-only patients compared with healthy controls. The data are biologically plausible, statistically robust against multiple-testing correction, and consistent with an expanding international literature linking trace-element deficiency with cardiometabolic disease. Serum zinc assessment should be incorporated into the routine metabolic profiling of ACS patients as a simple, inexpensive means of identifying individuals requiring intensified cardiometabolic surveillance. Randomised controlled trials of zinc supplementation are needed to translate these epidemiological findings into definitive therapeutic guidelines.

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