Association of Zinc with New Generation Cardiovascular Risk Markers in Childhood Obesity

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***Abstract*—**Zinc (Zn) is a vital element required for growth and development particularly in children. It exhibits some protective effects against cardiovascular diseases (CVDs). Zn may be a potential biomarker of cardiovascular health. High sensitive cardiac troponin T (hs-cTnT) and cardiac myosin binding protein C (cMyBP-C) are new generation markers used for prediagnosis, diagnosis and prognosis of CVDs. The aim of this study is to determine Zn as well as new generation cardiac markers' profiles in children with normal body mass index (N-BMI), obese (OB), morbid obese (MO) children and children with metabolic syndrome (MetS) findings. The association among them will also be investigated. Four study groups were constituted. The study protocol was approved by the institutional Ethics Committee of Tekirdag Namik Kemal University. Parents of the participants filled informed consent forms to participate in the study. Group 1 is composed of 44 children with N-BMI. Group 2 and Group 3 comprised 43 OB and 45 MO children, respectively. 45 MO children with MetS findings were included in Group 4. World Health Organization age- and sex-adjusted BMI percentile tables were used to constitute groups. These values were 15-85, 95-99 and above 99 for N-BMI, OB and MO, respectively. Criteria for MetS findings were determined. Routine biochemical analyses including Zn were performed. hs-cTnT and cMyBP-C concentrations were measured by enzyme-linked immunosorbent assay. Data were analyzed by using SPSS software. $p < 0.05$ was accepted as significant. Four groups were matched for age and gender. Decreased Zn concentrations were measured in Groups 2, 3 and 4 compared to Group 1. Groups did not differ from one another in terms of hs-cTnT. There were statistically significant differences between cMyBP-C levels of MetS group and N-BMI as well as OB groups. There was an increasing trend going from N-BMI group to MetS group. There were statistically significant negative correlations between Zn and hs-cTnT as well as cMyBP-C concentrations in MetS group. In conclusion, inverse correlations detected between Zn and new generation cardiac markers (hs-TnT and cMyBP-C) have pointed out that decreased levels of Zn accompany increased levels of hs-cTnT as well as cMyBP-C in children with MetS. This finding emphasizes that both Zn and these new generation cardiac markers may be evaluated as biomarkers of cardiovascular health during severe childhood obesity precipitated with MetS findings and also suggested as the messengers of the future risk in the adulthood periods of children with MetS.

***Keywords*—**Cardiac myosin binding protein-C, cardiovascular diseases, children, high sensitive cardiac troponin T, obesity.

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I. Introduction

ZINC is one of the most essential micronutrients involved in numerous biological functions such as cell differentiation and proliferation, endocrine, immune, and central nervous system functioning, reproduction and homeostasis [1]. Zn was shown to possess adipotropic effects through the role of Zn transporters, Zn finger proteins, and Zn-α2-glycoprotein in adipose tissue physiology, underlying its particular role in obesity pathogenesis [2].

A significant part of biological effects of Zn is mediated by its antioxidant and anti-inflammatory roles [3]. Antioxidant functions of Zn may have various positive effects on cardiovascular health and could prevent the development of CVDs [4]. Zn supplementation ameliorated cardiac inflammation and hypertrophy [5]. Zn supplementation also improves body weight management, reduces anthropometric measurements and concentrations of inflammatory biomarkers in OB individuals [6].

Imbalances in Zn homeostasis as in the case of Zn deficiency contribute significantly to the development of CVDs [7]. Decreased serum Zn levels were observed in overweight and OB adults and children. It was suggested that while measuring BMI among OB children, monitoring Zn levels would also be plausible in order to avoid deficiency problems [8]-[10].

MetS is associated with hs-cTnT elevation. Increased circulating hs-cTnT concentrations were observed in children and adolescents with obesity and MetS. The MetS components have a cumulative impact on hs-cTnT levels in healthy individuals [11], [12].

cMyBP-C level may be a significant diagnostic and prognostic biomarker in children with heart failure and used as a marker of disease severity, because its level increases in these cases [13]-[15].

The role of Zn deficiency mechanisms in the pathogenesis of CVDs is still not known. Therefore, we aimed at evaluating the possible association between zinc and the new generation cardiac markers (hs-cTnT and cMyBP-C) in normal-BMI, OB, MO children and those with MetS.

II. Patients and Methods

A. Patients

177 children were recruited in the study. Informed consent forms were obtained from the parents of the participants. The institutional ethics committee approved the study protocol. Four groups were constituted. The first group comprised 44 children with N-BMI, second and third groups contained 43

OB and 45 MO children, respectively. Group 4 included 45 children with MetS. Tables for age- and sex-adjusted BMI percentiles prepared by World Health Organization were used for selection of patients [16]. Children with N-BMI (15^{th}-85^{th} percentiles) constituted Group I.

B. Anthropometric Measurements

Body weight, height, waist circumference, hip circumference, head circumference and neck circumference of the children were measured and recorded. BMI values were calculated.

C. Obesity Classification

Children with BMI-percentiles varying between 95 and 99 were included in Group 2, which was composed of OB children. MO children constituted Group 3. In this group, there were children with BMI percentiles above 99.

D. MetS Criteria

Children with central obesity, elevated systolic and diastolic blood pressure, high blood glucose values, increased triglyceride and/or decreased high density lipoprotein cholesterol (HDL-C) concentrations constituted Group 4, who were evaluated as the participants with MetS [17].

E. Laboratory Measurements

Routine laboratory tests including fasting blood glucose, blood lipids such as triglycerides and HDL-C were performed by autoanalyzer. Zn concentrations were measured. Cardiac markers', hs-cTnT and cMyBP-C, levels were determined using research kits working with enzyme-linked immunosorbent assay principle.

F. Statistical Analysis

Statistical package for social sciences software was used for the analysis of the study data. Descriptive statistics were performed. Mean ± standard deviation and median values were calculated. Analysis of variance and *post hoc* Tukey tests or Mann-Whitney-U and Kruskal-Wallis tests were performed where appropriate. p value smaller than 0.05 was accepted as statistically significant. Correlation tests were done. Linear regression plots with 95% mean prediction interval were drawn.

III. Results

Groups were matched in terms of their age and gender ratios. Mean age ± standard deviation values of the children in groups 1, 2, 3, and 4 were 10.9 ± 4.2 years, 12.1 ± 3.2 years, 10.6 ± 3.5 years and 12.1 ± 2.6 years ($p > 0.05$), respectively.

Table I showed BMI values and the results of the anthropometric measurements (waist, hip, head and neck circumferences) confined to each group. Statistically significant differences between the groups were also shown in the table.

Steady-state increases were observed in BMI values as well as the other anthropometric measurements of the groups ($p < 0.05$).

Serum zinc, hs-c TnT and cMyBP-C values were given in Table II.

TABLE I
BMI Values, Anthropometric Measurements of the Groups (mean ± SD)

Parameter		Group 1 N-BMI	Group 2 OB	Group 3 MO	Group 4 MetS
BMI	kg/m^2	17.6 ± 3.0	23.7 ± 3.4	27.6 ± 5.3	30.3 ± 4.7
Waist C	cm	64.8 ± 11.8	80.9 ± 8.4	88.2 ± 14.2	97.1 ± 10.4
Hip C	cm	77.4 ± 14.7	93.2 ± 11.9	97.0 ± 16.2	104.7 ± 14.3
Head C	cm	53.1 ± 2.7	54.5 ± 2.0	55.1 ± 2.3	55.4 ± 2.2
Neck C	cm	29.3 ± 3.8	32.9 ± 3.7	33.6 ± 3.8	35.7 ± 3.2

C = circumference

[BMI and waist C (Groups 1-2 < 0.001, 1-3 < 0.001, 1-4 < 0.001, 2-3 < 0.05, 2-4 < 0.001, 3-4 < 0.05), hip C (Groups 1-2 < 0.001, 1-3 < 0.001, 1-4 < 0.001, 2-4 < 0.01), head C (Groups 1-3 < 0.001, 1-4 < 0.001, 1-2 < 0.05), neck C (Groups 1-2 < 0.001, 1-3 < 0.001, 1-4 < 0.001, 2-4 < 0.01, 3-4 < 0.05)]

Zinc concentrations were decreased in OB and MO children compared to those in children with N-BMI ($p > 0.05$). No statistically significant difference was observed between the study groups in terms of hsTnT concentrations. Statistically significant increases were detected between Group 1 as well as Group 2 and Group 4 for cMyBP-C levels ($p < 0.05$).

Statistically significant negative correlations were found between Zn and hs-cTnT ($r = -0.356$; $p < 0.05$) as well as cMyBP-C ($r = -0.404$; $p < 0.05$) concentrations in MetS group. These associations were shown in Figs. 1 and 2, respectively.

TABLE II
The Concentrations of Zn, hs-cTnT, cMyBP-C of the Groups (mean ± SD)

Parameter		Group 1 N-BMI	Group 2 OB	Group 3 MO	Group 4 MetS
Zn	µg/dL	90.0 ± 18.3	84.6 ± 14.9	76.5 ± 25.5	76.6 ± 26.7
hsTnT ^{m}	ng/L	31.5	32.1	30.4	33.3
cMyBP-C $^{m\#}$	ng/mL	3.79	4.02	4.26	4.50

^{m} = median; [$^{\#}$ 1-4, 2-4 $p < 0.05$]

In other groups, significant correlations were not found among parameters.

IV. Discussion

Zn, as a physiologically essential element commonly measured by atomic absorption spectroscopy, is particularly important for children, because it is required for growth and development as well as cell structure and function. Therefore, an association between zinc deficiency and cell oxidative stress was introduced [4], [18], [19].

In a previous study performed on OB individuals, mean serum zinc was lower than the normal range [6]. In the present study, lower zinc levels were measured in OB, MO, and MetS groups compared to the values determined in N-BMI group.

Zn exhibits protective effects against CVDs [18]. Higher serum zinc levels were associated with lower risk of the development of CVDs [20]. Zn deficiency was suggested as a contributing factor for developing CVDs [1]. A significant association between low serum zinc levels and heart failure was reported [21]. Recently, Zn was introduced as a biomarker of cardiovascular health [1].

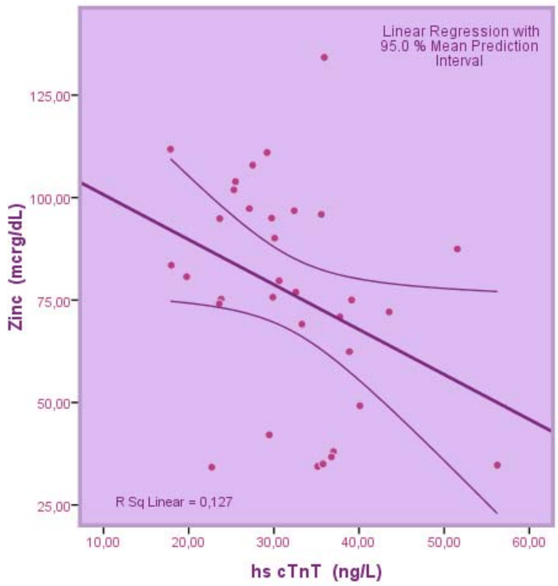

Fig. 1 Negative correlation between serum zinc values and hs-cTnT concentrations in MetS group

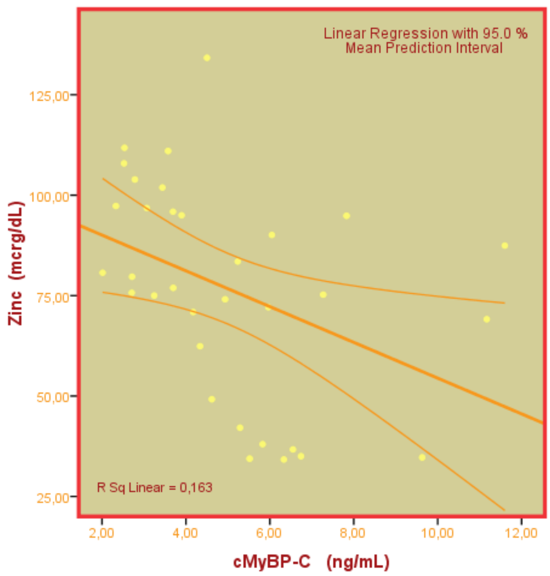

Fig. 2 Negative correlation between serum zinc values and cMyBP-C concentrations in MetS group

Cardiac markers are also being used to evaluate the status of cardiovascular health and diseases. In a study, zinc was found to be inversely correlated with creatine kinase, creatine kinase-MB and cTnT activities [22]. In another study performed on Egyptian children, higher cTnT, cTnI, creatine kinase-MB, lactate dehydrogenase values and lower Zn concentrations were found in children affected by scorpion sting envenomation. Cardiac markers were reported as the most important determining factor for the severity and the outcome of scorpion envenomation [23].

High sensitive-TnT was reported as the strong predictor of outcome in OB patients with heart failure [24]. Increased levels were also detected in OB MetS patients [11], [12].

In heart failure, cMyBP-C levels were also increased in children [13]-[15].

In this study, in MetS group, elevated hsTnT and cMyBPC levels were found in comparison with the levels measured in N-BMI group.

Zn levels were significantly inversely correlated with serum creatine kinase, creatine kinase-MB and cTnT levels. The prevalence rate of acute myocardial infarction decreased with increasing zinc quartiles [22].

In our study, negative correlation between zinc and hsTnT was observed in MetS group. Besides, we have also found another negative correlation between zinc and cMyBP-C levels in the same group.

V. Conclusion

In conclusion, Zn and both of these new generation cardiac markers may be introduced as markers for cardiovascular health among children with MetS. They may predict cardiovascular risk in the future lives of children in this group.

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