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ABSTRACT

Background: Ischemic heart disease (IHD) imposes an emerging epidemic globally and in Egypt. The role of zinc in ischemic heart disease wasn't well assessed. A limited number of researches explored serum zinc status in ischemic heart disease patients.

Objective: To explore differences in serum zinc level between IHD patients and control group.

Methodology: A case control study included 110 people aged ≥ 20 years old; 50 cases of ischemic heart disease diagnosed within the previous six months were recruited from Cardiology department and its outpatient clinic at Al-Zahraa University Hospital. Sixty controls were recruited from those without ischemic heart disease attending General surgery, Urology and Otorhinolaryngology clinics at the same hospital. Data were collected using an interviewer-administered questionnaire. Serum zinc of cases and controls was measured. SPSS version 20 was used for data analysis.

Results: Cases of ischemic heart disease had significantly lower serum zinc level as compared to controls ($P < 0.05$) with Odds Ratio (OR) = 3.33. Disaggregated data indicated that serum zinc was significantly lower among females with IHD but not males. The most significant ischemic heart disease risk factors were less education, positive family history of cardiovascular disease, smoking, less frequent consumption of dairy products and animal proteins, psychic tension, physical inactivity, short sleep hours, obesity and hypertension.

Conclusion: These findings suggest that serum zinc level might be associated with ischemic heart disease especially among females.

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INTRODUCTION

Ischemic heart disease (IHD) also known coronary heart disease is the most common form of cardiovascular disease (CVD) [1]. Globally, it is the foremost cause of death and disability. It is responsible for more than one-third of all mortality in people aged 35 and more [2]. Egypt ranks 15th globally in IHD mortality; the age adjusted death rate of IHD is 271.7 per 100,000. In 2018, IHD deaths reached 29.4% of total deaths [3].

Ischemic heart disease is a multifactorial disease and identifying its risk factors is of value in the prevention. As the well-known risk factors for IHD such

as hypertension, smoking and obesity only account for about half of its relative mortality, therefore, new ways of thinking about IHD are needed [4]. The relationship of dietary intake, particularly micronutrients, and the risk of cardiovascular disease has been an emerging area of investigation [5]. When micronutrients were investigated, there has been a growing interest in the role of minerals in IHD [6]. Of particular interest is zinc, because it acts as an antioxidant, anti-inflammatory and membrane stabilizer [7]. Zinc maintains cardiac stem cells essential for heart function [8]. The critical contribution of perturbations in zinc homeostasis to myocardial

ischaemia/reperfusion injury and the protective role of zinc signaling against cardiac injury were highlighted [9]. Recent evidence has pointed out an emergent role of zinc in IHD. Zinc deficiency can cause an increase in tissue oxidation damage. Hence, there is a rising concern about zinc implication in the pathogenesis of IHD [10].

The rising prevalence of IHD is causing much concern in the public health domain. On the other hand, data on zinc deficiency and its association with IHD are controversial and information is limited particularly in Egypt. Therefore, research on zinc in patients with IHD is important as this trace element may be useful predictor and its level might be adjusted to prevent IHD.

Research Question: Is there a difference between IHD patients and the control group as regards serum zinc level?. The null hypothesis (H_0) assumed that there is no difference between IHD patients and the control group as regards serum zinc level. This study was carried out to explore differences in serum zinc level between IHD patients and the control group.

SUBJECTS AND METHODS

Study Design and Setting: A Case control study was conducted over a period of 2 years from March 2019 to October 2021, cases of ischemic heart disease at Al-Zahraa University Hospital in Al-Abbassia-Cairo and controls from attendants without IHD at the same hospital. The study protocol was approved by ethical committee of faculty of medicine for girls, Cairo, Al-Azhar University and an oral informed consent from all subjects was obtained.

Cases were all patients visiting Cardiovascular department and its outpatient clinic in the hospital and newly diagnosed with IHD within the previous six months. Control group was attendants without IHD who were sex and age matched, eligible for the study and agreed to participate; they recruited from General surgery, Urology and Otorhinolaryngology outpatient clinics at the same hospital. The sample was drawn by visiting the selected clinics according to the scheduled clinic days.

Inclusion Criteria: Regarding cases: Both sexes of diagnosed IHD patients, aged 20 years and above were included in the study. Regarding controls: Attendants without IHD, aged 20 years and above of both sexes were included

Exclusion Criteria: Patients who are diabetics, have chronic diarrhea and/or receive zinc supplementation were excluded.

Diagnostic Criteria: For cases: Ischemic heart disease patients were diagnosed as per the Monica criteria [11]:(1) Two or more ECG showing specific changes; (2) An ECG showing probable changes plus abnormal cardiac

injury enzymes; or (3) Typical symptoms such as a retrosternal pain plus abnormal enzymes. **For controls:** A control was defined as an individual who attended the outpatient clinics of Al-Zahraa University Hospital for conditions other than angina pectoris and myocardial infarction. For the selection of proper control, person's history regarding ischemic heart disease was asked and it was assured that the control had never been admitted to hospital or taken treatment for acute myocardial infarction and angina pectoris. In addition, ECG was performed to them.

Sample Size

The required sample size was 80 (40 cases and 40 controls) and was calculated by Epi info version 7 with 95% confidence level, 80% power of study and 1:1 ratio of controls to cases. The researcher recruited 110 participants (50 cases and 60 controls).

Study Tools

- An interviewer-administered questionnaire was designed to include the following data:
- ***Socio-demographic data:** Age, sex, marital status, residence and education.
- ***Risk factors of ischemic heart disease:** family history of cardiovascular disease, sleep hours, smoking habits, physical activity using The General Practice Physical Activity Questionnaire [12], dietary habits of food elements rich in zinc as red meat, fish, oysters and crabs, poultry, various dairy products, legumes and nuts, psychic tension score using Stress and tension level test [13] as well as stressful life events such as death events and social problems.
- ***Associated comorbidities:** such as hypertension and anaemia.

Physical Examination:

- A. Anthropometric Measurements:** Body weight and height were measured. Body Mass Index (BMI) was then calculated. $BMI = \text{weight (kg)} / \text{height (meter)}^2$ [14]. Waist Circumference (WC) was measured in a standing position, midway between the inferior margin of lateral lower ribs and the iliac crests in a horizontal plan. The tape was fitted tightly without compressing the soft tissues [15].
- B. Blood Pressure Measurement:** Blood pressure was measured for cases and controls using a calibrated mercury sphygmomanometer in a sitting position with the forearm placed horizontal on the table after about five minutes rest [16].

Laboratory Tests:

All cases and controls were investigated for serum zinc level using Colorimetric test. Only five millilitres of peripheral blood were collected in a plain vacuum tube, allowed to clot at room temperature and the serum was separated by centrifugation. Zinc fluid mono-reagent was used for the determination of zinc in serum at wavelength 560 nm. The value for normal zinc level was 70–150

µg/dl. Classification of zinc, accordingly, was deficient (<70 U_g/dl), optimal (70-150 U_g/dl) and excess (>150 U_g/dl) [17].

Statistical analysis

The Statistical Package for Social Sciences (SPSS) version 20 was used for data entry and analysis. For a descriptive purpose, qualitative data were presented as frequencies and percentages; while means, standard deviations and ranges were used to describe quantitative variables. To assess the significance in the observed differences between cases and controls, Pearson's Chi-square Test for independence (χ^2) was used for qualitative categorical data and Fisher Exact Test was also done if any expected frequency was less than five. The Independent Student's t-Test was used for the differences between means of two continuous variables of unpaired groups. Odds Ratio (OR) was calculated. Pearson's correlation coefficient (r) was calculated to measure correlation between serum zinc and cardio-metabolic risk factors. Binary logistic regression and linear regression were also done. P-values were taken at a pre-determined threshold probability, the significance level of 0.05 and 95% confidence limit. The results were deemed to be statistically significant if the p-value (two-tailed) was < 0.05.

The mean age of IHD cases was 54.8±10.2 years and that of controls was 50.9±10.5 years. The proportion of males among cases were 54% as compared to 53.3% among controls. Regarding residence, 86% of cases compared to 52 % of controls resided in urban areas, with statistically significant difference (OR=5.02). Regarding marital status, widows were represented 28% among cases compared to 3.3% of controls with statistically significant difference. Regarding education, university degree was more among cases (20%) than controls (6.7%), with statistically significant difference. Statistically significant more cases than controls had positive family history of cardiovascular diseases. More cases were current smokers (46%), physically inactive (92.2%) and reported short sleep duration (<7 hours) (64%) as compared to controls (18.3%, 76.7% 36.7%, respectively). Psychic tension score, experience of death of close relatives and social problems were significantly higher among cases than controls (Table 1).

Regarding zinc rich food intake as dairy products (yogurt, milk and cheese) and animal protein (poultry and red meat), cases showed lower frequency of intake of such food items than controls. While, insignificant differences between them were found regarding the frequency of intake of fish, oysters and crabs, legumes and nuts (table 2).

RESULTS

Table (1): Lifestyle risk factors among cases of ischemic heart disease and controls

Studied groups Lifestyle risk factors	Cases (n=50)	Controls (n=60)	Stat. tests
	n (%)	n (%)	
Smoking habit:			Fisher's Exact=9.67
- Never smoker	24 (48.0)	43 (71.7)	P=0.007*
- Ex-smoker	3 (6.0)	6 (10.0)	OR**=2.74
- Current smoker	23 (46.0)	11 (18.3)	CI=1.2-6.0
Physical activity category *** :			$\chi^2=4.68$
- Inactive	46 (92.2)	46 (76.7)	P=0.030*
- Active	4 (8.0)	14 (23.3)	OR=3.50
			CI=1.1-11.4
Sleeping hours:			$\chi^2=9.71$
- < 7	32 (64.0)	22 (36.7)	P=0.008*
- 7-8	7 (14.0)	22 (36.7)	
- >8	11 (22.0)	16 (26.6)	
Psychic tension score:			t=3.49
- Mean ± SD	6.82±1.72	5.82±1.28	P=0.001*
- Range:	5 (5-10)	5 (5-10)	
Stressful life events			$\chi^2=16.05$
1-Death of close relatives:			P=0.000*
- Present	14 (28.0)	1 (1.7)	OR=22.94
- Absent	36 (72.0)	59 (98.3)	CI=2.8-181.9
2-Social problems:			$\chi^2=10.48$
- Present	12 (24.0)	2 (3.3)	P=0.001*
- Absent	38 (76.0)	58 (96.7)	OR=9.15
			CI=1.9-43.2

SD: Standard deviation, χ^2 : chi square test, OR: Odds ratio, C.I.: Confidence interval, t: Independent t test, *: Significant p-value, **To perform dummy variable ex and current smokers were summed, ***These categories were done using The General Practice Physical Activity Questionnaire [12].

Table (2): Zinc rich food intake among cases of ischemic heart disease and controls

Frequency of food intake	Cases (n=50)	Controls (n=60)	Stat. tests
	n (%)	n (%)	
Red meat:			
- Monthly	18 (36.0)	19 (31.7)	$\chi^2 = 6.28$ P =0.043*
- Once/week	24 (48.0)	19 (31.7)	
- >1 time /week	8 (16.0)	22 (36.6)	
Fish, oysters and crabs:			
- Monthly	20 (40.0)	34 (56.7)	$\chi^2 = 5.55$ P =0.062
- Once/week	26 (52.0)	18 (30.0)	
- >1 time /week	4 (8.0)	8 (13.3)	
Poultry:			
- Monthly	12 (24.0)	3 (5.0)	$\chi^2 = 8.60$ P =0.013*
- Once/week	18 (36.0)	30 (50.0)	
- >1 time /week	20 (40.0)	27 (45.0)	
Yogurt:			
- Monthly	28 (56.0)	21 (35.0)	$\chi^2 =11.16$ P =0.011*
- ≤ 4 times/week	14 (28.0)	19 (31.6)	
- > 4 time /week	0 (0.0)	10 (16.7)	
- Daily	8 (16.0)	10 (16.7)	
Milk:			
- Monthly	19 (38.0)	9 (15.0)	$\chi^2 = 16.02$ P =0.001*
- ≤ 4 times/week	17 (34.0)	24 (40.0)	
- > 4 time /week	0 (0.0)	12 (20.0)	
- Daily	14 (28.0)	15 (25.0)	
Cheese:			
- Monthly	8 (16.0)	4 (6.7)	$\chi^2 = 12.40$ P =0.005*
- ≤ 4 times/week	24 (48.0)	24 (40.0)	
- > 4 time /week	2 (4.0)	17 (28.3)	
- Daily	16 (32.0)	15 (25.0)	
Legumes:			
- Monthly	11 (22.0)	6 (10.0)	$\chi^2 = 4.63$ P =0.208
- Once/week	7 (14.0)	5 (8.3)	
- >1 time /week	13 (26.0)	22 (36.7)	
- Daily	19 (38.0)	27 (45.0)	
Nuts:			
- < 1/Month	45 (90.0)	47 (78.3)	$\chi^2 =2.71$ P =0.100
- ≥ 1/Month	5 (10.0)	13 (21.7)	

χ^2 : Chi square test, *: Significant p-value

More cases had history of anemia than controls. The means of body mass index, waist circumference, systolic blood pressure and diastolic blood pressure were statistically significant higher among cases comparing to controls (table 3). The mean serum zinc level among cases (85.6±40.4 Ug/dl) was lower than controls (109.8±49.2 Ug/dl). More cases (40%) had deficient zinc level than controls (16.7%). Those with low serum zinc level were at risk for IHD three times more than those of high level. These differences were statistically significant (table 4). Disaggregating data, sex-wise distribution of serum zinc level among cases of ischemic heart disease and controls revealed lower serum zinc in female cases. Female cases had statistically significant lower serum zinc level comparing to controls. However, among males no statistical significant difference was found between cases and controls (table 5). In cases, serum zinc level

was negatively correlated with psychic tension score, body mass index, waist circumference and diastolic blood pressure (table 6). It was found that the most relevant predictors for lower serum zinc level using linear regression model were anemia, being diagnosed with IHD, short sleep hours and old age. Among cases, urban residence, anemia, increased waist circumference and old age were the most significant predictors to lower serum zinc level, while female sex, physical inactivity and smoking were not a relevant predictors to serum zinc using linear regression model (table 7). The most relevant predicting factors related to higher ischemic heart disease using logistic regression were female sex, urban residence, family history of cardiovascular disease, smoking, higher systolic blood pressure, deaths of close relatives, social problems, higher psychic tension score and lower serum zinc level (table 8).

Table (3): History of anemia and anthropometric and blood pressure measurements of cases of ischemic heart disease and controls

Factor	Studied groups	Cases (n=50)	Controls (n=60)	Significant tests
		n (%)	n (%)	
Anemia:				
- Present		21 (42.0)	1 (1.7)	$\chi^2 = 27.73$ P=0.000*
- Absent		29 (58.0)	59 (98.3)	
BMI (Kg/m²):				
- Mean ± SD		30±4.9	27.3±4.7	t=3.05 P=0.003*
- Range		(18.5-43)	(18.5-43.8)	
Waist circumference (cm):				
- Mean ± SD		99.2±14.8	90.4±13.7	t=3.27 P=0.003*
- Range		73(66-139)	54 (65-119)	
Systolic blood pressure (mmHg):				
- Mean ± SD		133.1±18.9	119.2±12.9	t=4.56 P=0.000*
- Range		80 (90-170)	50(100-150)	
Diastolic blood pressure (mmHg):				
- Mean ± SD		83.4±12.5	77.8±11.0	t=2.47 P=0.015*
- Range		40 (60-100)	40 (60-100)	

SD= Standard deviation, t=Independent t test, *: Significant p-value

Table (4): Serum zinc level among cases of ischemic heart disease and controls

Serum zinc	Studied groups	Cases (n=50)	Controls (n=60)	Significant tests
		n (%)	n (%)	
Classification of zinc (Ug/dl):				
- Deficient (<70)		20 (40.0)	10 (16.7)	$\chi^2 = 8.89$ P=0.012* OR=3.33 CI=1.4-8.1
- Optimal (70-150)		28 (56.0)	42 (70.0)	
- Excess (>150)		2 (4.0)	8 (13.3)	
Serum zinc level (Ug/dl):				
- Mean ± SD		85.6±40.4	109.8±49.2	t=2.78 P=0.006*
- Range		135 (25-160)	253 (27-280)	

χ^2 = chi square test, OR= Odds ratio, C.I=Confidence interval, t=Independent t test, *Significant P value (<0.05).

Table (5): Sex-wise distribution of serum zinc level among cases of ischemic heart disease and controls

Serum zinc	Sex	Males		Females	
		Cases (n=27)	Controls (n=32)	Cases (n=23)	Controls (n=28)
		n (%)	n (%)	n (%)	n (%)
Serum zinc level:					
- <70 Ug/dl		9 (33.3)	7 (21.9)	11 (47.8)	3 (10.7)
- ≥70 Ug/dl		18 (66.7)	25 (78.1)	12 (52.2)	25 (89.3)
Significant statistical test		$\chi^2=1.64$ P=0.200		$\chi^2=6.84$ P=0.009*	

χ^2 : Chi square test, *: Significant p-value

Table (6): Correlation between cardio-metabolic factors and serum zinc level among cases of ischemic heart disease

Factors	r	P value
Sleep duration	0.19	0.199
Psychic tension score	-0.40	0.004*
Body mass index	-0.28	0.046*
Waist circumference	-0.46	0.001*
Diastolic blood pressure	-0.30	0.032*

r:Pearson's correlation *: Significant p-value

Table (7): Linear regression for predictors of serum zinc level

Predictors	Unstandardized B Coefficients	P value	95%CI for B	
			Lower	Upper
Among cases of ischemic heart disease and controls:				
Age	0.97	0.017*	0.18	1.75
Ischemic heart disease	-22.15	0.025*	-41.42	-2.87
Sleep duration	-6.45	0.006*	-11.04	-1.88
Anemia	-26.19	0.028*	-49.54	-2.88
Constant	-133.99	0.000		
Among cases of ischemic heart disease:				
Age	1.02	0.048*	0.01	22.03
Female sex	1.86	0.912	-9.71	35.45
Urban residence	61.03	0.000*	28.74	93.31
Smoking	9.22	0.330	-9.65	28.09
Physical inactivity	-19.68	0.254	-54.03	14.66
Waist circumference	-1.56	0.000*	0.84	2.28
Anemia	-33.04	0.002*	-53.31	-12.77
Constant	-168.89	0.015		

*: Significant p-value

Table (8): Logistic regression for predictors of risk factors of ischemic heart disease

Predictors	B Coefficients	Wald	P value	OR	95%CI for OR	
					Lower	Upper
Female sex	1.88	4.86	0.027*	6.57	1.23	35.08
Urban residence	3.20	7.95	0.005*	24.62	2.65	228.13
Family history of cardiovascular disease	2.56	9.39	0.002*	12.95	2.52	66,67
Systolic blood pressure	0.08	8.50	0.004*	1.08	1.03	1.13
Deaths of close relatives	5.93	9.94	0.002*	374.37	9.42	1068.8
Social problems	3.54	6.33	0.011*	34.34	2.19	539.37
Psychic tension score	0.707	6.41	0.011*	2.03	1.17	3.50
Serum zinc level	-0.020	4.39	0.036*	0.98	0.96	0.99
Constant	34.23	21.17	0.000			

*: Significant p-value

DISCUSSION

The expanding IHD epidemic increases along with increasing prevalence of its risk factors [16]. So, it seems crucial to examine these risk factors. Zinc status may contribute to the development of IHD. A direct association between serum zinc and cardio-metabolic risk factors is recently suggested [18].

Studying the socio- demographic context revealed that widow state, urban residence and high educational degree were more in cases than controls. Previous studies show that being widowed and divorced exhibited a greater coronary risk than being never-married and married [19,20]. Psychological stressors, behavioral and socioeconomic factors may play a role in such relation. Urban residence was further confirmed to be a relevant IHD predictor. Stressful life, physical inactivity, unhealthy diet and environmental factors as noise and pollution in the urban areas may explain the current findings. Similar urban rural difference was also observed by Ram & Trivedi [21]; Taha [22] and Omran et al [23]. However, O'Connor &

Wellenius [24] showed that IHD was higher among rural dwellers. Previous studies' findings regarding education were controversial, in agreement with our results, Mohanan et al [25] clarified that high educational class represents important socioeconomic risk factors for IHD. This association may be mediated by lifestyle risk factors such as sedentary behaviors and more stress.

Regarding serum zinc, our results denoted that high prevalence of zinc deficiency was detected among IHD cases as compared with their controls. Serum zinc level was also a relevant predictor of IHD. Similarly, several studies reported a statistically significant lower serum zinc in IHD patients as compared to their controls [26-32]. On contrary, other studies found that serum zinc concentration is less insignificantly in IHD patients as compared to controls [8,33-36].

A worthy note is the observed sex-difference. In females, serum zinc was lower among cases than controls. While

among males, lack of such zinc-IHD relationship was showed. In accordance, Alissa et al^[37] who reported that serum zinc concentrations didn't differ between males with and without IHD. However, they didn't examine females. In general, biological, cultural, dietary, behavioral, psychological and socioeconomic factors may exhibit an important role in sex difference. The sex difference in the current study supported the suggested role for hormones in the regulation of zinc transporter mRNA expression^[38].

Lifestyle factors were found to influence serum zinc^[39]. Short sleep hours, current smoking as well as physical inactivity were more in the studied cases than controls. Besides, zinc was associated with short sleep hours; whereas both physical activity and smoking weren't a relevant serum zinc predictors. Similar relationship between zinc and sleep is found in general population^[40], women^[41] and children in early adolescence^[42]. Bediz et al^[43] found that melatonin hormone, which regulates sleep cycle, increases zinc levels when its level is optimal in case of sufficient sleep. Regarding smoking, our finding is in line with Ding et al^[44] who elicits that current and ex tobacco smoking are important risk factors for IHD. Lack of association between zinc and smoking may be explained by the finding that nearly half of the studied cases and controls were females who culturally unacceptable for them to be seen smokers. Physical inactivity which observed among the studied cases is supported by Mohan and Deepa^[45] and Ram & Trivedi^[21] who clarify that the decrease of physical activity explains the escalation of IHD. The attitude of Egyptian towards avoiding exercise because of various socio-cultural factors^[46] may alter the association between physical activity and zinc in the present study.

In the present study, cases and controls had clear differences in dietary patterns which could be the associates of the observed difference in their serum zinc level. Animal protein (poultry and red meat) and various dairy products (yogurt, milk and cheese), vegetables and fruits were consumed less frequently by cases as compared to controls. These differences were in agreement with previous researches^[32,47].

From psychological point of view, cases had more psychic tension and experienced stressful life events more than controls. Psychic tension is an independent factor predicting IHD. Together, El-Moselhy et al^[48] show that stress is a major risk factor for IHD. Research has cleared the importance of stress caused by acute and chronic life events in IHD^[49]. Serum zinc level was associated with psychic tension score among the studied cases. The suggested mechanism may be that exposure to psychological stress decreases extracellular zinc level through glucocorticoid-mediated metallothionein synthesis^[50].

Concerning medical risk factors, history of anemia, BMI, WC and both systolic and diastolic blood pressure were higher among cases than controls. In addition, anaemia, obesity and hypertension were associated with serum zinc. This result is in line with Ibrahim et al^[51] and Taha^[22] who showed that hypertension is more prevalent among Egyptian IHD patients. It is well established that cardiovascular peptides which regulate blood pressure are zinc-dependent which could explain zinc association with blood pressure^[52]. Also, Li et al^[53] stated that obesity and abdominal obesity are IHD risk factors. Furthermore, Rahbar-Taramsari et al^[32] found that serum zinc was associated with body weight among patients with cardiovascular disease. The inflammation promotes zinc accumulation in the liver and in adipocytes, which may contribute to the negative association of serum zinc level with BMI and WC in obese individuals^[54]. Changes in zinc status with anaemia are frequently explained by coexisting deficiencies of iron and zinc due to the common dietary sources of both micronutrients and decreasing their intestinal absorption by the same dietary factors^[55].

CONCLUSION

According to the previous discussion, we can conclude that this study provide a reasonable evidence for the association between decreased level of serum zinc and IHD especially among females. There is a still need for more information and better understanding of this relation. The field of micronutrients is needed to be an explicit component of health research, interventions and system reform, education, policies and programs.

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REFERENCES

1. **World Health Organization (WHO).** Cardiovascular diseases fact sheet. [[https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-\(c\)](https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(c))]. Accessed October, 2021.
2. **Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, Cheng S, et al.** American Heart Association Council on epidemiology and prevention statistics committee and stroke statistics subcommittee. Heart disease and stroke statistics-2018 update: a report from the American Heart Association. *Circulation*. 2018;137 (12): e67–e492.
3. **World Health Rankings 2018.** Egypt, coronary heart disease. [<https://www.worldlifeexpectancy.com/egypt-coronary-heart-disease/>]. Accessed October, 2021.

4. **Essien OE, Andy J, Ansa V, Out AA and Udoh A.** Coronary artery disease and the profile of cardiovascular risk factors in South Nigeria: a clinical and autopsy study. *Cardiol. Res. Pract.* 2014; (2014).
5. **Chu A, Foster M and Samman S.** Zinc status and risk of cardiovascular diseases and type 2 diabetes mellitus-A systematic review of prospective cohort studies. *Nutrients.* 2016;8(11): 707.
6. **Hashemian M, Poustchi H, Abnet CC, Boffetta P, Dawsey SM, Brennan PJ, Pharoah P, et al.** Dietary intake of minerals and risk of esophageal squamous cell carcinoma: results from the Golestan Cohort Study. *Am J Clin Nutr.* 2015;102(1): 102–8.
7. **Lee SR.** Critical role of zinc as either an antioxidant or a prooxidant in cellular systems. *Oxidative Medicine and Cellular Longevity.* 2018; 9156285: 11.
8. **Islamoglu Y, Evliyaoglu O, Tekbas E, Cil H, Mehmet E, Zuhail A, et al.** The relationship between serum levels of zinc and Cu and severity of coronary atherosclerosis. *Biol Trace Elem Res.* 2011;144: 436-44.
9. **Chasapis CT, Loutsidou AC, Spiliopoulou CA and Stefanidou ME.** Zinc and human health: An update. *Arch. Toxicol.* 2012; 86: 521–534.
10. **Anonna SN, Ahamed SK, Uddin G, Adnan T, Uddin N, Hussain S, et al.** A clinical evaluation of the alterations in the level of serum zinc, copper, iron, and manganese in the ischemic heart disease patients of Bangladesh – A case-control study. *Heliyon.* 2020; 6 (10): e05311.
11. **World Health Organization (WHO). Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, Arveiler D, Rajakangas AM and Pajak A.** Myocardial infarction and coronary deaths in the World Health Organization MONICA Project. Registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. *Circulation.* 1994; 90:583-612.
12. **National Health Service England 2009.** The general practice physical activity questionnaire (GPPAQ): A screening tool to assess adult physical activity levels, within primary care. [https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/192453/GPPAQ_-_guidance.pdf]. Accessed October, 2021.
13. **Farquhar JW.** Stress and tension level test in Thaxton NA. *Pathways to fitness.* Harper & Row Publ., New York, 1978.
14. **World Health Organization (WHO) 2006.** Obesity and overweight Fact sheet No.311. [<http://www.who.int/mediacentre/factsheets/fs311/en/index.html>]. Accessed October, 2021.
15. **World Health Organization (WHO) 2008.** Waist circumference and waist-hip ratio : report of a WHO expert consultation, Geneva, 8-11. [<https://apps.who.int/iris/handle/10665/44583>]. Accessed October, 2021.
16. **Pickering TG, Hall JE, Appel L, Falkner B, Graves J, Hill M, et al.** Response to recommendations for blood pressure measurement in human and experimental animals; Part 1: blood pressure measurement in humans and miscuffing: A Problem With New Guidelines: Addendum. *Hypertension.* 2006; 48 (Issue 1): e5-e6.
17. **Johnsen O and Eliasson R.** Evaluation of a commercially available kit for the colorimetric determination of zinc in human seminal plasma. *Int J Androl.* 10 (2):435-440, 1987.
18. **Knez M and Glibetic M.** Zinc as a biomarker of cardiovascular health. *Frontiers in Nutrition.* 2021;8:451.
19. **Ernstsen L, Bjerkeset O and Krokstad S.** Educational inequalities in ischaemic heart disease mortality in 44,000 Norwegian women and men: The influence of psychosocial and behavioural factors. *The HUNT Study Scandinavian Journal of Public Health.* 2010; 38 (7): 678–685.
20. **Dhindsa D S, Khambhati J, Schultz WM, Tahhan AS and Quyyumi AA.** Marital status and outcomes in patients with cardiovascular disease. *Trends in Cardiovascular Medicine.* 2020;30 (4): 215-220.
21. **Ram RV and Trivedi AV.** Behavioural risk factors of coronary artery disease: A paired matched case control study. *J Cardiovasc Dis Res.* 2012;3 (3): 212-217.
22. **Taha M.** Demographic profile and prevalence of risk factors among patients with coronary artery disease attending Bab El-Sheria University Hospital. Master Thesis in Community Medicine, Faculty of Medicine, Al- Azhar University, 2016.
23. **Omran MH, El-Sayed AA and Ezzat MAW.** Urban and rural differences of macrovascular complications prevalence among diabetic patients in Sohag governorate. *Sohag medical journal.* 2020;24 (1):155-160.
24. **O'Connor A and Wellenius G.** Rural urban disparities in the prevalence of diabetes and coronary heart disease. *Public Health.* 2012;126 (10): 813-20.
25. **Mohanan PP, Mathew R, Harikrishnan S, Krishnan MN, Zachariah G, Joseph J, et al.** Presentation, management, and outcomes of 25748 acute coronary syndrome admissions in Kerala, India. *Eur Heart J.* 2013;34 (2): 121-9.
26. **Kazemi-Bajestani SMR, Ghayour-Mobarhan M, Ebrahimi M, Moohebaty M, Esmaeili HA, Parizadeh M R, et al.** A Serum copper and zinc concentrations are lower in Iranian patients with angiographically defined coronary artery disease than in subjects with a normal angiogram. *Journal of Trace Elements in Medicine and Biology.* 2007;21 (1): 22–28.
27. **Kazi TG, Afridi HI, Kazi N, Jamali MK, Arain MB, Sarfraz RA, et al.** Distribution of zinc, copper and iron in biological samples of Pakistani myocardial infarction (1st, 2nd and 3rd heart attack) patients and controls. *Clin Chim Acta.* 2008;389 (1-2): 114–119.

28. **Hsieh BT, Chang CY, Chang YC and Cheng KY.** Relationship between the level of essential metal elements in human hair and coronary heart disease. *J Radioanal Nucl Chem.* 2011;290 (1): 165-169.
29. **Chhabra N, Kukreja S, Chhabra S, Chhabra S and Ramessur K, et al.** Is zinc deficiency an independent risk factor in the causation of ischemic heart disease? A case control prospective study to estimate serum zinc levels in patients of ischemic heart disease. *Web med Central biochemistry.* 2012;3(9): WMC003695.
30. **Bayir A, Kara H, Kiyici A, Oztürk B and Akyürek F.** Levels of selenium, zinc, copper, and cardiac troponin I in serum of patients with acute coronary syndrome. *Biol Trace Elem Res.* 2013;154 (3): 352–6.
31. **Nazir S, Ullah E, Hussain S and Bukharir R.** A study of serum zinc levels among patients of coronary artery disease conducted in a tertiary care hospital. *Biomedica.* 2013;29 (3): 137-138.
32. **Rahbar-Taramsari, M, Mahdaviroshan, M, Shahd B, Sadegi M and Shakiba M.** Zinc status in cardiovascular patients in the North of Islamic Republic of Iran . *Journal of Paramedical Sciences (JPS).* 2013;4(3):68-74.
33. **Tan C, Chen H and Xia C.** The prediction of cardiovascular disease based on trace element contents in hair and a classifier of boosting decision stumps. *Biol. Trace Elem. Res.* 2009;129 (1): 9–19.
34. **Giannoglou GD, Konstantinou DM, Kovatsi L, Chatzizisis YS and Mikhailidis DP.** Association of reduced zinc status with angiographically severe coronary atherosclerosis: a pilot study. *Angiology.* 2010; 61(5): 449–55.
35. **Afridi HI, Kazi TG, Kazi N, Kandhro G A , Jameel K, Baig A, et al.** Interactions between cadmium and zinc in the biological samples of Pakistani smokers and nonsmokers cardiovascular disease patients. *Biol Trace Elem Res.* 2011;139(3): 257–68.
36. **Cebi A, Kaya Y, Gungor H, Demir H, Yoruk IH, Soylemez N, et al.** Trace elements, heavy metals and vitamin levels in patients with coronary artery disease. *Int J Med Sci.* 2011;8(6): 456–60.
37. **Alissa E, Bahjri S and Ahmed W.** Trace element status in Saudi patients with established atherosclerosis. *J Trace Elem Med Biol,* 2006;20 (2): 105–114.
38. **Liuzzi JP and Cousins RJ.** Mammalian zinc transporters. *Annu Rev Nutr.* 2004;24: 151–72.
39. **Vashum KP, McEvoy M, Milton AH, Islam MR, Hancock S and Attia J.** Is serum zinc associated with pancreatic beta cell function and insulin sensitivity in pre-diabetic and normal individuals? Findings from the Hunter Community Study. *PLoS ONE.* 2014;24: 151–72.
40. **Grandner MA, Jackson N, Gerstner JR and Knutson KL.** Dietary nutrients associated with short and long sleep duration. Data from a nationally representative sample. *Appetite.* 2013;64: 71-80.
41. **Song CH, Kim YH and Jung KI.** Associations of zinc and copper levels in serum and hair with sleep duration in adult women. *Biol Trace Elem Res.* 2012;149 (1): 16–21.
42. **Ji X and Liu J.** Associations between blood zinc concentrations and sleep quality in childhood: a cohort study. *Nutrients.* 2015;7 (7): 5684–5696.
43. **Bediz CS, Battaci AK and Morgulkoc R.** Both zinc deficiency and supplementation affect plasma melatonin levels in rats. *Acta physiologica Hungarica.* 2003;90 (4): 335-9.
44. **Ding N, Sang Y, Chen J, Ballew SH, Kalbaugh CA, Salameh MJ, et al.** Cigarette smoking, smoking cessation, and long-term risk of 3 major atherosclerotic diseases. *Journal of the American College of Cardiology.* 2019;74 (4): 498-507.
45. **Mohan V and Deepa R.** Risk factors for coronary artery disease in Indians. *The Journal of the Association of Physicians of India (JAPI).* 2004;52: 95-7.
46. **Hegazi R, El-Gamal M., Abdel-Hady N and Hamdy O.** Epidemiology of and risk factors for type 2 diabetes in Egypt. *Annals of Global Health.* 2015;81 (6): 814 – 820.
47. **Maher MA and Gutbi SS.** Assessment of dietary pattern among coronary heart disease outpatients attended El-Shaap teaching hospital, Khartoum state. 2013; Dis. 3: 7-14.
48. **El-Moselhy EA, Mohammed, A-ES, Abd El-Aziz A, Sadek I , Hagrass SA and Farag GAS.** Coronary artery disease among elderly egyptian patients: I. Socio-demographic, lifestyle, psychosocial, medical, and biochemical risk factors. *Am J Gerontol Geriatr.* 2018;1(2): 1006.
49. **Khayyam-Nekouei Z, Neshatdoost H, Yousefy A, Sadeghi A and Manshaee G.** Psychological factors and coronary heart disease. *ARYA Atheroscler.* 2013; 9(1): 102-9.
50. **Tian X, Zheng Y and Li Y.** Psychological stress induced zinc accumulation and up-regulation of ZIP14 and metallothionein in rat liver. *BMC Gastroenterology.* 2014;14: 3217.
51. **Ibrahim MM, Ibrahim A, Shaheen K and Nour MA.** Lipid profile in Egyptian patients with coronary artery disease. *Egyptian Heart J.* 2013;65 (2): 79-85.
52. **Mousavi SM, Mofrad MD and Borges do Nascimento IJ.** The effect of zinc supplementation on blood pressure: a systematic review and dose–response meta-analysis of randomized-controlled trials. *European Journal of Nutrition.* 2020;59: 1815–1827.
53. **Li C, Ma R, Zhang, X, Ma J, Wang X, He J, et al.** Risk of coronary heart disease in the rural population in Xinjiang: A nested case-control study in China. *PLoS ONE.* 2020;15(3): e0229598.
54. **Zaky DSE, Sultan EA, Salim MF and Dawod RS.** Zinc level and obesity. *Egypt J Intern.* 2013;25 (4): 209–212.

55. **Lind T.** Iron and zinc in infancy: Results from experimental trials in Sweden and Indonesia. Umea

University Medical Dissertations. 2004; 87: 1–108.

الملخص العربي

دراسة الحالات والشواهد على داء القلب الإقفاري والزنك في مصل الدم بمستشفى الزهراء الجامعي
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ملخص البحث:

الخلفية: يعتبر مرض القلب الإقفاري وباءً متصاعداً على مستوى العالم وفي مصر. إن علاقة الزنك بداء القلب الإقفاري لم يتم تقييمها بشكل جيد. قام عدد محدود من الأبحاث بدراسة الزنك في مصل الدم لدى مرضى داء القلب الإقفاري.

الهدف: الهدف الرئيسي من هذه الدراسة هو استكشاف الاختلافات في مستوى الزنك بين مرضى داء القلب الإقفاري ومجموعة الشواهد.

الطرق: أجريت دراسة حالات وشواهد على 110 من الأشخاص البالغين ≤ 20 عاماً؛ 50 حالة تعاني من داء القلب الإقفاري تم تشخيصها في خلال ست شهور سابقة ومن المترددين على العيادة الخارجية وقسم القلب والأوعية الدموية بمستشفى الزهراء الجامعي. كما تضمنت الدراسة 60 شخص في مجموعة الشواهد الخاليين من داء القلب الإقفاري المترددين على العيادات الخارجية الأخرى بنفس المستشفى. تم جمع البيانات عن طريق استبيان. تم قياس مستوى الزنك في مصل الدم لجميع الحالات والشواهد التي تم دراستها. تم استخدام الحزمة الإحصائية للعلوم الاجتماعية لإدخال البيانات وتحليلها.

النتائج: كان مستوى الزنك في الدم لدى حالات داء القلب الإقفاري أقل مقارنة بالشواهد مع وجود دلالة إحصائية و نسبة الأرجحية ($OR = 3.33$). عند عمل مقارنة لمستوى الزنك للذكور والإناث كل على حدة كان الفرق ذو دلالة إحصائية فقط لدى الإناث. كانت أهم عوامل خطر للإصابة بداء القلب الإقفاري هي قلة التعليم، والتاريخ العائلي الإيجابي لأمراض القلب والأوعية الدموية، والتدخين، والاستهلاك الأقل لمنتجات الألبان والخضروات والبروتينات الحيوانية، والتوتر النفسي، وقلة النشاط البدني، وقلة ساعات النوم، والسمنة وارتفاع ضغط الدم.

الاستنتاجات: تشير هذه النتائج إلى أن مستوى الزنك في الدم قد يكون مرتبطاً بداء القلب الإقفاري خاصة لدى الإناث. هناك حاجة إلى مزيد من البحث في الفروق بين الجنسين في هذه العلاقة.

الكلمات المفتاحية: داء القلب الإقفاري، الزنك في مصل الدم، أمراض القلب والأوعية الدموية، دراسة حالات وشواهد.

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