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Original Article

Serum level of Selenium, Zinc, and Vitamin C and their relation to the clinical spectrum of leprosy

Hesham N Khalid[1], Mohammed I Mostafa[2], Nayrah Saad Attia[3], Heba Allah Saad Eldeen Bazid[1]

[1] *Dermatology and Andrology Department, Faculty of Medicine, Menoufia University, Egypt*
[2] *Clinical Pathology Department, Medical Research Division, National Research Center, Egypt*
[3] *Kafr El Sheikh Dermatology and Leprosy Hospital, Kafr El Sheikh, Egypt*

Abstract

Introduction: Leprosy is a chronic infectious disease with many risk factors including inadequate nutrient intake and nutritional deficiencies, which affect the immune system, and influence leprosy progression.

Objectives: To elucidate the relation between the serum level of zinc, vitamin C, and selenium and the clinical spectrum of leprosy.

Methodology: A case control study included 100 leprotic patients (50 multibacillary and 50 paucibacillary) and 100 age and sex matched controls. Vitamin C was measured by ELISA, zinc was measured by using centronic colorimetric spectrophotometry, and selenium was measured by Inductivity Coupled Plasma Optical Emission Spectroscopy technique.

Results: Zinc and Vitamin C levels were significantly lower in paucibacillary (mean ± SD = 89.86 ± 20.712 and 2.52 ± 1.27 respectively) and multibacillary (mean ± SD = 81.41 ± 18.61 and 1.98 ± 0.59 respectively) than in controls (mean ± SD = 107.34 ± 3.98 and 4.95 ± 2.45 respectively) (p value < 0.001) with no significant difference between paucibacillary and multibacillary patients (p value = 0.142 and = 0.066 respectively). Selenium level showed no significant difference between the three groups (p value > 0.05) (mean ± SD = 51.27 ± 42.61 in paucibacillary, 47.54 ± 30.21 in multibacillary, and 44.07 ± 46.58 in controls).

Conclusions: Lower serum levels of zinc and vitamin C in leprosy patients may be a result of disease pathogenesis or related to the antioxidants based treatment. It might also present prior to the disease onset due to malnutrition that may have accelerated the development of leprosy.

Key words: leprosy; vitamin C; zinc; selenium.

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Introduction

Leprosy, also known as Hansen's disease, is a chronic infection caused by *M. leprae* bacteria which primarily targets the skin, peripheral nerves [1]. It is an obligate intracellular pathogen that infects macrophages and Schwann cells of the peripheral nervous system [2]. Leprosy has a wide range of clinical manifestations, which may be progressive and cause permanent damage if left without treatment. Based on the bacillary load, leprosy is classified as paucibacillary (PB) and multibacillary (MB) forms [3]. PB leprosy is a mild form with two to five pale or reddish skin patches, whereas MB consists of more than five skin lesions, nodules, plaques, thickened dermis, or skin infiltration [4]. The spectrum of clinical forms directed by the patient's immune response towards the *M. leprae* is broad; it ranges from the tuberculoid pole with well-behaved cell-mediated immunity, few lesions, and bacilli to the lepromatous pole with humbled immunity paired with wide-spread lesions and more bacillary load. In between, the borderline group lies with three subdivisions: borderline tuberculoid (BT), mid borderline (BB), and borderline lepromatous (BL) [3].

In addition, various systemic manifestations of leprosy can be observed; one of them is the otorhinological manifestation which is common towards the lepromatous pole of the disease. In fact, stuffiness is one important nasal symptom preceding skin lesions which may alert clinicians and this may lead to possible early diagnosis of lepromatous leprosy (LL), together with blood-stained nasal/postnasal discharge, and epistaxis. Due to this fact, meticulous examination of the nasal area should be part of every examination of the leprosy patient especially when suspecting the BL or LL form of leprosy [5]. Although epistaxis is not very common, it is important for early diagnosis of MB leprosy. It is often a result of nasal blockage, thick discharge, and ulceration, and sometimes septal perforation. It may also occur that leprosy affects the arteriovenous complex of the nasal mucosa, exaggerating pre-existing local pathology. Although it is usually minimal, epistaxis may

sometimes take an unpredictable course in advanced leprosy and may even be life-threatening [6].

Although the number of new cases decreased globally according to WHO records, it is still a public health problem especially in the developing areas around the world. To date, the risk factors of the transmission of *M. leprae* and the development of leprosy cannot be fully understood. The long incubation period is considered one of the reasons that makes it difficult to investigate causal relationships between the circumstances at the time of infection and the onset of clinical symptoms years later [7]. The association between poverty and leprosy has been recognized for a long time, with several associated variables that include agglomeration, low educational level, low nutritive diet, and social inequality [8]. Egypt is considered to be one of those developing countries in which leprosy is still endemic, probably due to the fact that Egypt is currently one of the nations with the largest total number of people living in poverty among the Middle East and North African countries [9]. Nutritional deficiencies are common in countries in which leprosy is endemic. In Egypt, malnutrition is reported mostly in the form of overweight and obesity, which increased in prevalence over the last 20 years due to high caloric diets and sedentary lifestyles. Furthermore, different deficiency micronutrients such as zinc and selenium have been reported [10]. Thus, the clinical presentation of the disease is a result of nutritional deficiencies as well as other environmental and genetic factors in the host.

Nutrition is known to influence immune response in several aspects. Deficiency of trace elements and vitamins affect the innate and adaptive immune response, causing an unbalance of the host response to pathogens [11]. Zinc deficiency provokes a deficiency of Th1 response with reduction of cytokines, such as IFN-γ, IL-2, and TNF-α that are important for the control of intracellular pathogens, such as *M. leprae*. Moreover, selenium deficiency results in impaired phagocytic and lymphocytic activity [12], and vitamin C stimulates production, function, and movement of leukocytes (e.g., neutrophils and phagocytes) and has roles in lymphocyte differentiation and proliferation [13]. These micronutrients also have an important role as antioxidants since all of them are involved in the oxidant defence network that protects the cell membrane from oxidative damage caused by reactive oxygen species (ROS) released during bacterial phagocytosis [14].

Hence, our study aims to elucidate the relation between the serum level of zinc, vitamin C, and selenium and the clinical spectrum of leprosy.

Methodology

A total number of 200 individuals were included in this case control study: 100 leprotic patients (50 MB and 50 PB) and 100 age and sex-matched healthy controls. All cases were randomly selected from the Outpatient Clinic of Kafr El Sheikh Dermatology and Leprosy Hospital. The sample size estimation based on the review of past literature (Arora *et al*. [15]) found that the mean serum zinc level was significantly lower in leprosy cases than in control cases: 85.9 ± 26.9, respectively. The sample was calculated at power 80% and confidence level 95%. It was assumed that 180 subjects will be recruited to detect this difference; the sample was increased to 200 participants to avoid dropouts and it was divided into two groups.

Ethical considerations

Prior to the collection of the samples, written informed consent was obtained from all studied subjects, and the Local Ethics Committee of Research involving human subjects at the Faculty of Medicine, Menoufia University, Egypt, approved this study (record number: 19519DERM), in agreement with the Declaration of Helsinki (World Medical Assembly).

Exclusion criteria

Patients were excluded from the study if they had a history of antioxidants consumption or had any other chronic or granulomatous disease.

All the patients were initially diagnosed by their clinical features by a referral centre and then referred to our hospital, where they were examined by a dermatologist and subjected to the following: taking their full history (personal history, history of the present illness, nutritional history, medical history, and past history), complete general examination (vital signs, face examination, eye examination, nose examination, and mouth examination), nerve examination for tenderness or enlargement at suspected areas, and dermatological examination (skin texture, sensation, color and hair growth at suspected lesions), as well as examination of macules, patches, nodules, and ulcers if present. Then, slit skin smear was done to confirm the diagnosis and determine the clinical spectrum of the disease according to the bacterial index.

Microbiological examination by slit skin smears

The samples were taken from earlobes and from the rim of the lesion in PB patients and from the centre of the lesion in MB patients. The bacilli were counted and graded according to a logarithmic scale (bacillary index: BI) and the percentage of the solid bacteria that was considered living (viable) bacilli was estimated (morphological index: MI) [16].

Laboratory investigations

Venous blood samples were drawn under aseptic conditions in sterile tubes. Tubes were centrifuged, and about 2 mL of serum was collected and stored at minus 20 ºC for selenium, zinc, and vitamin C measurements. All laboratory measurements were carried out in the Clinical Pathology Department Laboratories, Medical Research Division, National Research Center, Cairo, Egypt. Vitamin C measurement was done using SunRed Human (VC) ELISA Kit catalogue no. 201-12-1539, Ref: DZE201121539, Lot: 202001 (SunRed-Bio, Meilan building, 6497 HuTai Road, Baoshan District, Shanghai, China). Zinc was measured using centronic colorimetric zinc fluid monoreagent Kit, Ref ZF01000050, Lot ZF01191C6I (centronic GmbH, AM Kleinfeld 11, 85456 Wartenberg, Germany). Selenium was measured using the Inductivity Coupled Plasma Optical Emission Spectroscopy (ICP-OES) technique using Agilent 5100 Dual View ICP-OES instrument (Agilent technologies, 5301 Stevens Creek Blvd, Santa Clara, California, USA).

Statistical analysis of the data

All data underwent collection, tabulation, and statistical analysis by an IBM personal computer with Statistical Package of Social Science (SPSS) version 22 (SPSS, Inc, Chicago, Illinois, USA), where the following statistics were used: descriptive statistics, in the form of range, mean, and standard deviation (SD), presented the quantitative data, and the qualitative data were presented in the form of percentages and numbers.

Analytical statistics were used to detect the possible correlation between the targeted disease and studied factors. The used tests of significance included the following: Chi-square test (χ^2) was used to study the correlation between two qualitative variables, Mann-Whitney test U (nonparametric) was used to compare between two groups that are not normally distributed having quantitative variables, Kruskal-Wallis test (nonparametric) was used to compare between three or more groups that are not normally distributed having quantitative variables, and Spearman's correlation (r) was used to measure the association between quantitative and qualitative ordinal variables. Student t-test was used for normally distributed quantitative variables to compare between two studied groups. Pearson coefficient was used to correlate between two normally distributed quantitative variables. The cut-off value with the highest accuracy was selected as the diagnostic cut-off points: p value < 0.001 was considered statistically highly significant; p value <

Table 1. Sociodemographic data of studied groups.

	Cases (N = 100)		Control (No = 100)		Test of sig.	p
	N	%	N	%		
Sex						
Male	45	45.0	33	33.0	χ^2 = 3,026	0.082
Female	55	55.0	67	67.0		
Age (years)						
Min. – Max.	19.0 – 64.0		31.0 – 61.0			
Mean ± SD.	42.55 ± 14.72		39.45 ± 9.68		t = 1.760	0.080
Median (IQR)	43.50 (28.50 – 57.50)		35.0 (33.50 – 40.0)			
BMI (kg/m^2)						
Min. – Max.	18.92 – 33.29		19.25 – 31.10			
Mean ± SD.	26.16 ± 3.95		26.37 ± 3.33		t = 0.419	0.676
Median (IQR)	26.55 (23.39 – 29.38)		27.55 (24.42 – 29.17)			
Nutrional status						
Average	100	100.0	100	100.0	–	–
Comorbidities						
No	100	100.0	100	100.0	–	–
Yes	0	0.0	0	0.0		
Socioeconomic						
Low	100	100.0	100	100.0	–	–
Therapy used						
No	0	0.0	-	-	–	–
MDT	100	100.0	-	-		

PB: paucibacillary; MB: multibacillary; χ^2: Chi square test; t: Student t-test; p: p value for comparing between the two studied groups.

0.05 was considered significant; p value > 0.05 was considered nonsignificant.

Ethical statement

Prior to the collection of samples, written informed consent was obtained from all studied subjects, and the Local Ethics Committee of Research involving human subjects in the Faculty of Medicine, Menoufia University approved this study; record number: 19519DERM41, in agreement with the Declaration of Helsinki (World Medical Assembly).

Results

The mean age of leprosy patients was 42.55 ± 14.72 and 55% of them were females, while the mean age of the control group was 39.45 ± 9.68 years and 67% of them were females. The body mass index of leprosy patients ranged between 18.92 and 33.29 with a mean level of 42.55 ± 14.72, and in the controls, it ranged from 19.25 to 31.10 with a mean level of 39.45 ± 9.68. The nutritional status of both leprosy patients and controls was average, and the socioeconomic standard was low in both groups. There were no associated comorbidities in both studied groups. The patients were on multidrug therapy (MDT) (Table 1).

The clinical examination of the cases revealed that, in PB patients, 90% had hypopigmented macules with weak sensation and 10% had erythematous patch with weak sensation, and also one nerve damage was observed in 20% of the PB patients. While in the MB group of patients 90% had skin lesions: macules and nodules represented 30% of the lesions, nodules and infiltration were observed in 20%, nodules and ulcers were found in 20%, macules and patches were found in 10%, and ulcers and patches were present in 10%. Only 10% of the patients presented with epistaxis and no skin lesions. Concerning the nerves that were damaged in MB patients, 90% had nerve damage (10% had only one damaged nerve, 40% had two damaged nerves, 30% had three damaged nerves, and 10% had four damaged nerves) (Table 2).

Slit skin smear in both groups of leprosy patients revealed that 100% of PB leprosy cases had negative smears, and 100% of MB leprosy cases had positive smears with different results by slit skin smear, which were as follows: +1 in five cases (10%), +2 in ten cases (20%), +3 in ten cases (20%), +4 in ten cases (20%), and +5 in fifteen cases (30%) (Table 3).

By comparing the three studied groups with traced elements, the results showed that the serum level of zinc was significantly lower in PB as it ranged from 65.8 to 129.4, with a mean level of 89.86 ± 20.71, while in MB, it ranged from 50.6 to 110.60, with a mean level of 81.41 ± 18.61, when compared to healthy controls, the values ranged from 78.5 to 169 with a mean level of 107.34 ± 23.98 and the p value was < 0.001, with no significant difference between PB and MB patients with p value = 0.142.

Table 2. Clinical data in both groups of leprosy patients.

Clinical data	Total (N = 100)		Type of leprosy			
			PB (N = 50)		MB (N = 50)	
	N	%	N	%	N	%
Skin lesion						
Absent	5	5.0	0	0.0	5	10.0
Present	95	95.0	50	100.0	45	90.0
Erythematous patch with weak sensation	45	5.0	1	10.0	0	0.0
Hypopigmented macules with weak sensation	15	45.0	9	90.0	0	0.0
Macules-nodules	15	15.0	0	0.0	15	30.0
Macules-patches	5	5.0	0	0.0	5	10.0
Nodules- infiltration	10	10.0	0	0.0	10	20.0
Nodules –ulcer	10	10.0	0	0.0	10	20.0
patches –ulcers	5	5.0	0	0.0	5	10.0
Epistaxis						
Absent	95	95.0	50	100.0	45	90.0
Present	5	5.0	0	0.0	5	10.0
Nerve damage						
Absent	45	45.0	40	80.0	5	10.0
Present	55	55.0	10	20.0	45	90.0
One nerve	15	15.0	10	20.0	5	10.0
Two nerves	20	20.0	0	0.0	20	40.0
Three nerves	15	15.0	0	0.0	15	30.0
Four nerves	5	5.0	0	0.0	5	10.0

PB: paucibacillary; MB: multibacillary.

Table 3. Slit skin smear in both groups of leprosy.

Slit skin smear	Total (N = 100)		Type of leprosy			
			PB (N = 50)		MB (N = 50)	
	N	%	N	%	N	%
None	50	50.0	50	100.0	0	0.0
+1	5	5.0	0	0.0	5	10.0
+2	10	10.0	0	0.0	10	20.0
+3	10	10.0	0	0.0	10	20.0
+4	10	10.0	0	0.0	10	20.0
+5	15	15.0	0	0.0	15	30.0

PB: paucibacillary; MB: multibacillary.

Table 4. Comparison between the three studied groups according to three trace elements.

	Type of leprosy (N = 100)		Control (N = 100)	*p*
	PB (N = 50)	MB (N = 50)		
Zinc				
Range	65.80 – 129.40	50.60 – 110.60	78.50 – 169.0	$p_1 = 0.142$
Mean ± SD	89.86 ± 20.71	81.41 ± 18.61	107.34 ± 23.98	$p_2 < 0.001^*$
Median (IQR)	83.50 (75.3 – 101.2)	85.30 (65.8 – 96.5)	99.65 (89.05 – 119.8)	$p_3 < 0.001^*$
Selenium				
Range	1.0 – 127.10	1.0 – 95.20	1.0 – 145.20	$p_1 = 0.488$
Mean ± SD	51.27 ± 42.61	47.54 ± 30.21	44.07 ± 46.58	$p_2 = 0.340$
Median (IQR)	50.85 (11.6 – 85.6)	50.55 (27.5 – 70)	25.0 (6.30 – 81.80)	$p_3 = 0.132$
VitC				
Range	1.0 – 4.80	1.30 – 2.90	1.0 – 7.40	$p_1 = 0.066$
Mean ± SD	2.52 ± 1.27	1.98 ± 0.59	4.95 ± 2.45	$p_2 < 0.001^*$
Median (IQR)	2.10 (1.40 – 3.50)	1.90(1.40 – 2.50)	6.35 (2.35 – 7.25)	$p_3 < 0.001^*$

PB: paucibacillary; MB: multibacillary. p_1: *p* value for Mann Whitney test for comparing between PB and MB; p_2: *p* value for Mann Whitney test for comparing between PB and Control; p_3: *p* value for Mann Whitney test for comparing between MB and Control; *: Statistically significant at $p \leq 0.05$.

Table 5. Correlation between the three markers in leprosy patients.

	Zinc		Selenium	
	r_s	p	r_s	p
Cases (N = 100)				
Selenium	0.089	0.377		
VitC	0.177	0.078	-0.032	0.750
PB (N = 50)				
Selenium	0.083	0.568		
VitC	0.175	0.224	-0.140	0.331
MB (N = 50)				
Selenium	0.238	0.096		
VitC	0.220	0.125	-0.049	0.736

r_s: Spearman coefficient; MB: multibacillary; PB: paucibacillary. *: Statistically significant at $p \leq 0.05$.

Table 6. Relation between age, sex and three markers.

	Zinc		Selenium		VitC	
	Median (Range)	Mean ± SD.	Median (Range)	Mean ± SD	Median (Range)	Mean ± SD
Sex						
Male (n = 45)	82.3 (50.6 – 101.2)	80.1 ± 15.1	56.0 (1- 95.2)	57.1 ± 28.8	2.4 (1.3 – 4.8)	2.4 ± 1.1
Female (n = 55)	84.7 (50.6 – 129.4)	90.2 ± 22.4	40.1 (1-127.1)	43.1 ± 41.4	1.8(1 – 4.3)	2.1 ± 1
U (*p*)	965.00 (0.059)		967.50 (0.060)		1044.00 (0.178)	
Age	r (*p*)= -0.132 (0.192)		r (*p*) = 0.164 (0.102)		r (*p*) = -0.026 (0.801)	

U: Mann Whitney test; r: Pearson coefficient; *p*: *p* value for comparing between the two categories.

The serum level of vitamin C was also significantly lower in PB as it ranged from 1 to 4.8 with a mean level of 2.52 ± 1.27, and in MB, it ranged from 1.3 to 2.90 with a mean level of 1.98 ± 0.59, when compared to healthy controls that ranged from 1 to 7.4, with a mean level of 4.95 ± 2.45 and the *p* value was < 0.001, with no significant difference between PB and MB patients with *p* value = 0.066. The serum level of selenium ranged from 1 to 127.10 with a mean level of 51.27 ± 42.61 in PB cases, while it ranged from 1 to 95.20 with a mean level of 47.54 ± 30.21 in MB cases. However, in the healthy control group, the selenium level ranged from 1 to 145.2 with a mean level of 44.07 ± 46.58. No significant difference was found regarding serum selenium level between MB and controls, PB and controls, and PB and MB and the *p* values were = 0.340, 0.132, and 0.488, respectively (Table 4).

There was no significant correlation between the three markers (Table 5). There was also no significant relation between the three markers and all the following parameters: sociodemographic data, clinical data, and slit skin smear (Tables 6–8).

Discussion

The exact role of malnutrition on susceptibility to leprosy and the development of a clinical stage remain unclear, which makes it difficult to determine if leprosy is a cause or a consequence of nutritional deficiencies [11].

Malnutrition deficiency, especially involving micronutrients, may accelerate leprosy development as it suppresses the immune response by affecting physical barriers (skin/mucosa), cellular immunity, and antibody production [17]. On the other hand, when leprosy develops, it may lead to micronutrient deficiency through their exhaustion as antioxidants [17]. In fact, several studies demonstrated the increased oxidative stress in leprosy [14].

This study measured the serum level of zinc, vitamin C, and selenium, which are considered important not only as antioxidants, but also as influencers of the immune response in several aspects. In addition, the study tried to assess the relation between their levels and the clinical spectrum of leprosy.

As far as zinc is concerned, there were significant differences regarding the serum zinc level between MB and controls and PB and controls, respectively, with no significant difference between MB and PB. This agreed with Arora *et al*. [15] who found significantly lower zinc level in leprosy cases as compared to controls ($p < 0.001$), while there was no significant difference between MB and BP; conversely that was in conflict with the study of Jain *et al*. [18] in which there was a

Table 7. Relation between three markers with type of Lesion and Epistaxis in cases group (n = 100).

	N	Zinc		Selenium		VitC	
		Median (Range)	Mean ± SD	Median (Range)	Mean ± SD	Median (Range)	Mean ± SD
Lesion							
Erythematous patch with weak sensation	5	82.3 (65.8-84.7)	76.2 ± 9.5	61.6 (1.0-84.8)	58.8 ± 34.3	2.4 (1.8 – 4.8)	3.2 ± 1.4
Hypopigmented macules with weak sensation	45	82.3 (65.8- 129.4)	87.4 ± 18.1	61.6 (1.0-127.1)	51.0 ± 39.6	1.8 (1.0 – 4.8)	2.3 ± 1.2
Macules-nodules	15	96.5 (50.6-129.4)	94.2 ± 26.8	39.5 (1.0-127.1)	48.5 ± 36.6	2.0 (1.4 – 4.3)	2.4 ± 0.9
Macules-patches	5	65.8 (62.3-100.0)	78.1 ± 20.1	1.0 (1.0 – 81.9)	33.4 ± 44.3	2.3 (1.3 – 2.9)	2.1 ± 0.8
Nodules-infilteration	10	95.9 (62.3-110.6)	87.3 ± 20.0	51.7 (1.0 – 81.9)	45.5 ± 33.7	2.3 (1.3 – 2.9)	2.1 ± 0.7
Nodules-ulcer	10	65.9 (62.3-91.8)	75.5 ± 14.1	70.2 (1.0 – 95.2)	52.5 ± 46.9	1.8 (1.3 – 2.8)	1.8 ± 0.6
Weak sensation –ulcer	5	50.6 (50.6-110.6)	74.6 ± 32.9	27.5 (27.5-58.2)	39.8 ± 16.8	2.4 (1.4 – 2.4)	2.2 ± 0.4
H (*p*)		8.734 (0.189)		3.134 (0.792)		5.898 (0.435)	
Epistaxis							
No	95	82.3 (50.6 – 129.4)	85.4 ± 20.6	45.1 (1.0 – 127.1)	49.1 ± 37.7	2.0 (1.0 – 4.8)	2.3 ± 1.0
Yes	5	89.4 (89.4 – 89.4)	89.4 ± 0.0	56.0 (56.0 – 56.0)	56.0 ± 0.0	1.5 (1.5 – 2.5)	1.7 ± 0.4
U(p)		175.0 (0.322)		225.0 (0.843)		191.50 (0.465)	

PB: paucibacillary; MB: multibacillary; H: H for Kruskal Wallis test; U: Mann Whitney test; *p*: *p* value for association between different categories; *: Statistically significant at $p \leq 0.05$.

Table 8. Correlation between Nerve damage, Slit skin smear and three markers in cases group (N = 100).

	Nerve damage		Slit skin smear	
	r_s	*p*	r_s	*p*
Zinc	-0.019	-0.019	-0.002	0.987
Selenium	-0.109	0.279	-0.103	0.307
Vit C	-0.191	0.057	-0.166	0.098

r_s: Spearman coefficient; *p*: *p* value for association between different categories.

gradual reduction in serum zinc concentrations as severity moved from tuberculoid leprosy (TL) to LL ($p < 0.001$).

Low serum zinc level in leprosy is considered a multifactorial deficiency to which several factors have been attributed, such as non-specific metabolic consequence of skin disease, probably due to consumption of body zinc by lepra bacilli [15]. Other authors found a relation between zinc deficiency and the release of leucocyte endogenous mediators due to continuous phagocytosis by macrophages that leads to redistribution of zinc and other metals from blood to various tissues [18]. Another reason is hypoalbuminemia that is associated with leprosy and may lead to hypozincemia [17].

All factors mentioned above can explain low serum zinc levels in leprosy patients. Also zinc deficiency in both types of leprosy might be due to dietary factors as leprosy is often associated with undernutrition [19]. As the body can't store zinc, a continuous steady intake of zinc is necessary and thus zinc deficiency might be common [20]. Also, a diet rich in phytate and low in animal proteins, which is common in the majority of developing countries, where leprosy mostly prevails, predisposes to insufficient intake and absorption of zinc [21]. This might explain how the Egyptian diet would contribute to zinc deficiency: although the whole wheat bread is an important component of the Egyptian diet and provides a large proportion of the daily caloric intake, it also contains large quantities of phytate [22]. This is in accordance with the study by Hassan *et al*. [23] who reported low serum zinc levels among Egyptians while conducting the national survey to determine mineral bone density in Egypt. A role might be played by increasing oxidative stress, which may exhaust antioxidants [24].

In our study, serum level of vitamin C showed a significant decrease in both MB and PB compared to healthy controls; this was observed in the study by Osadolor *et al*. [24] in which there was a significant decrease in the plasma vitamin C ($p < 0.05$) in patients with leprosy compared to the controls. In contrast to our results, Asalkar *et al*. [25] and Trimbake *et al*. [26] both found statistically significant decrease of vitamin C in LL patients with p values < 0.05 and < 0.001, respectively, while mean values remained the same in case of TT and control subsets.

The cause of this might be related to the fact that cases were newly diagnosed in those studies, while in our study not all of them were newly diagnosed, which may explain an increase in oxidative stress [24]. Furthermore, undernutrition reported in leprotic patients may be a contributing factor to low vitamin C in the serum as leprotic patients consume products that are deficient in vitamin C [4,7].

Selenium is an essential trace element, which has antiproliferative and immune-modulating properties. The key role of selenium in human metabolism is attributed to its presence in the glutathione peroxidase, which protects cells against harmful effects of free radicals [27].

In the present study, serum selenium level in the three studied groups showed no significant difference and that was against the results from the study by Partogi *et al*. [27] who found that the selenium level was significantly lower in MB than in PB. On the contrary, our results matched those by Olivera *et al*. [28], whose study showed that the selenium level was of no difference between leprotic patients and normal healthy controls. Concerning the low serum selenium level, levels in controls matched with those investigated by Samir *et al*. [29] whose study was done in Egypt and showed low serum selenium level among controls compared to the serum selenium level in other countries. Interestingly, they suggested that Egypt is a low selenium area and that may help in giving an explanation for such variations of selenium levels in the three studied groups, as they may consume food with different contents of selenium. In addition, it is known that serum selenium differs according to recent exposure which changes geographically and depends on the soil and water characteristics, as well as on the use of fertilizers containing selenium [30]. Thus, it makes it possible for the dietary intake of selenium to vary widely worldwide, according to its concentrations in plant-based nutrition and in animal sources of food, which in turn depends upon the selenium content of the plants used for forage, or whether animal food was fortified with selenium [31].

Likewise, there are other components that influence the selenium content of food as cultivation, climatic conditions, breeding methods, and methods of preparing food products [32]. Unfortunately, in many countries all over the world, human food ingredients do not provide sufficient selenium. In addition, the data concerning selenium content in food composition tables is often poor and depends on whether analysis is up to date and to what extent natural variability in selenium content is considered [33]. Concerning Egypt, few data are available concerning selenium content in common food types consumed by Egyptians; for instance, in the study by Hussein *et al*. [34] and Moatkhef *et al*. [33], some food types were rich in selenium, while others were deficient even though this cannot explain

selenium deficiency among Egyptians without estimation of dietary reference intake [34]. Moreover, many foods might be imported from a variety of different sources, which makes it difficult or impossible to determine the dietary intake of selenium only from food, which is local in origin [35]. All factors that have been mentioned may give us a clue to explain these results, but we still need further studies and systematic reviews originating from Egypt to estimate the dietary reference intake of selenium and consequently its value among serum in Egyptians.

Conclusions

Lower serum level of zinc and vitamin C in leprosy patients may be a result of disease pathogenesis or its treatment based on antioxidants, or it might have affected the patients since the beginning due to malnutrition that may accelerate the development of leprosy levels. Further studies on serum selenium are warranted.

Limitations

- Lack of sufficient data regarding the required daily intake of selenium among Egyptians.
- Limited number of patients included in the study.
- The leprotic patients were not newly diagnosed.

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Corresponding author

Heba Allah Saad Eldeen Bazid, MD
Dermatology and Andrology Department, Faculty of Medicine, Menoufia University, 93 Misrwa Elsudanstreat, 11646, Cairo, Egypt
Phone: +01090229191
Email: drhebasaadeldeen@hotmail.com

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