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SERUM LEVELS OF SELENIUM IN UNCOMPLICATED TYPE-2 DIABETIC PATIENTS AND HEALTHY INDIVIDUALS

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ABSTRACT: Selenium (Se) plays a vital role in maintaining the body's homeostasis. Selenoproteins have been found to play an integral role in the body's defense against oxidative stress. Type-2 diabetes mellitus is considered as an inflammatory state with high oxidative load and is one of the major chronic diseases prevalent in Pakistan. Serum levels of selenium in type 2 diabetic patients and healthy individuals were determined. The sample size consisted of 120 subjects. Inductively coupled plasma optical emission spectrometry was used for the serum selenium determination. Statistical analysis was done at the confidence interval (CI) of 95%. No significant difference was determined in the mean serum selenium levels of type 2 diabetic patients and healthy persons. Moreover, the studied population was observed to be selenium-replete population. Hence, laboratory evidence for prescribing selenium supplement is of vital importance and requires extreme care irrespective of the involvement of oxidative stress disease.

INTRODUCTION: Selenium is an essential trace element for the maintenance of homeostasis in the body [1]. Se is found in both organic and inorganic form in the environment. Selenium content of plant and animal food, dietary sources of Se, depends upon the concentration of soil in which they are grown. Selenium, being an important constituent of antioxidant enzymes (selenoproteins) like glutathione peroxidases, superoxide dismutases, thioredoxin reductases, protects against different deleterious effects of free radicals by modulating and participating in various physiological activities.

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Selenium plays an important role in normal thyroid function, enhancing immune function, protection against various types of cancer, in the prevention of pre-eclampsia, diabetes mellitus and male reproduction, *etc*.[2, 3, 4] Type 2 diabetes mellitus represents 90-95% of the diagnosed cases of diabetes [5]. Type-2 diabetes mellitus is considered an inflammatory state with a high oxidative load. The hyperglycemia causes alterations in the antioxidant defense system [6, 7].

Oxidative stress plays an important role in the pathogenesis of diabetes and shows an association with the development of secondary complications of diabetes [8, 9]. It has been proposed that the requirement of antioxidants may be more in diabetic patients compared to healthy individuals due to reduced efficiency of antioxidant system [10, 11, 12, 13].

The existing data all over the world about the relationship between serum selenium levels and type-2 diabetes is conflicting. No data of this relationship in the Pakistani population has yet been reported [10].

Therefore, this study was designed to determine the serum selenium levels of diabetic patients in the local region and compare them with those of healthy subjects.

METHODOLOGY: The study was approved by the Ethical committee of Services Hospital and the board of studies of Lahore College for Women University (LCWU). A sample size of the study was 120, encompassing 50 healthy volunteers and 70 type-2 diabetic patients with moderate or good glycemic control. Recruited subjects were declared healthy based on clinical examination and history. Subjects had an age range of 20-80 years.

Pregnant and lactating mothers, patients with end-stage renal disease, patients with any evidence of previously diagnosed liver disease and poorly controlled diabetics or those taking insulin were excluded from the study. Diabetic patients visiting the Diabetes Management Center (DMC) of a tertiary care hospital (Services Hospital) were recruited, after convenient random sampling.

Patients meeting the inclusion criteria were recalled on a later date in fasting state. Healthy individuals, meeting the inclusion criteria, were recruited as controls from a local university situated in close geographical proximity to DMC. Informed consent was acquired according to the guidelines set in the Helsinki Declaration. A structurally designed data collection form was used to gather information about the demographics, Physical Parameters, and medications of the recruited persons. Personal interview was used to aid the data collection form.

Blood samples (5ml) were collected and centrifuged at 3200 rpm for 15 min at 2-4 ºC. Serum was separated and then stored at -20 ºC until the time of analysis. All the biological wastes were destroyed according to hospital waste management protocol. The glassware used for analysis were previously soaked in 5 % nitric acid and then rinsed thoroughly with deionized water and oven dried at 100 ºC to exclude the possibility of mineral contamination.

The serum sample was thawed to room temperature at the time of analysis. 1 ml serum sample was taken and then diluted up to 25 ml with 0.1% (v/v) Triton-X 100 and 5% (v/v) HNO_3 (1:24). Accu stock solutions were used as standards. Perkin Elmer 5300 DV ICP-OES was used for the analysis of selenium in the serum. The wavelength used was 196.06 nm.

Statistical analysis was done by keeping the confidence interval (CI) at 95%. Differences in the serum selenium concentration between diabetic and healthy populations were analyzed with Student's t-test. Chi-square, ANOVA, and Kendall's tau b test were other tests used for statistical analysis. P-values of less than 0.05 were considered significant.

RESULTS: The study comprised a sample size of 120 subjects. 70 out of 120, typed 2 diabetic patients and 50 were healthy individuals. Among healthy subjects, 28 were female, and while among diabetic patients, 39 were female patients. The mean age of the recruited healthy subjects and diabetic patients was 35.9 $\pm$ 1.85 years and 49.44 $\pm$ 1.217 years, respectively **Table 1**.

The BMI, waist to hip ratio, fasting blood glucose, systolic blood pressure, and pulse data are given in **Table 2**. The diabetic patients had significantly higher fasting blood glucose and BMI than healthy individuals. ($p<0.05$) Mean serum selenium levels of healthy volunteers and diabetic patients were 530.40 ± 23.36 µg/L and 580.64 ± 20.20 µg/L, respectively.

The serum selenium concentration decreased with the progression of age in healthy individuals. ($p<0.05$) Paradoxically in diabetic patients, serum selenium levels, and age showed no association. ($p=0.147$) The age wise breakup of selenium levels is given in **Table 3**. The subjects were divided into quintiles according to age, and on comparing serum selenium levels in highest and lowest age quintiles, a statistically significant difference was observed in the healthy volunteers ($p<0.05$) but not in type-2 diabetic patients ($p=0.328$).

The results showed a significant difference in the serum selenium levels of healthy male (571.38 ± 32.84 µg/L) and healthy female subjects (478.25 ± 29.97 µg/L). ($p<0.05$) but no such gender

difference was observed in the serum selenium levels of diabetic patients. (p = 0.556). The diabetic female subjects had higher serum selenium levels (569.92 ± 28.01 µg/L) than the healthy female subjects (p<0.05) while male diabetics did not differ from healthy males **Table 4**.

TABLE 1: DESCRIPTIVE DATA SHOWING NUMBER OF SUBJECTS WHEN GROUPED ACCORDING TO A SPECIFIC TRAIT

Data	Diabetics n=70 (%)	Healthy n= 50 (%)
Gender		
Male	31 (44.28)	28 (56)
Female	39 (55.72)	22 (44)
Age groups (Years)		
20-38	10 (14.28)	34 (68)
39-56	45 (64.29)	11 (22)
57-75	15 (21.43)	05 (10)
Duration of Diabetes (Years)		
< 5years	46(65.7)	Nil
≥5years	24(32.3)	Nil
Tea Consumers (No. of cups)		
Occasional	15 (21.4)	12 (24)
1-2	47 (67.2)	18 (36)
3-4	08 (11.4)	20 (40)
Smoking		
Non-smokers	68 (97)	36 (72)
Smokers	02 (3)	14 (28)

TABLE 2: DETERMINATION OF ANTHROPOMETRIC PARAMETERS EXPRESSED AS MEAN ± STANDARD ERROR MEAN

Subjects		Age (Years)	BMI Kg/m^2	W/H ratio	BSF mg/dL	Pulse (min^{-1})	Systolic B.P (mmHg)	Diastolic B.P (mmHg)
Healthy	Overall	35.9±1.85	23.97±0.49	0.92±0.01	82.66±1.04	78.42±0.59	115.4±1.41	75.84±1.11
	Male	37±2.82	23.57±0.68	0.97±0.01	80.93±1.33	80.18±1.04	119.3±1.83	78.46±1.18
	Female	34.50±2.12	24.48±0.73	0.85±0.02	84.86±1.54	76.18±0.44	110.4±1.74	72.5±1.82
Diabetics	Overall	49.44±1.22	28.32±0.51	0.95±0.00	152.3±5.22	79.77±0.51	121.9±1.45	78.07±0.82
	Male	51.52±1.65	26.92±0.63	0.97±0.00	153.9±8.58	80.48±0.62	124.8±2.54	80.32±1.16
	Female	47.79±1.71	29.44±0.73	0.93±0.01	151.0±6.52	79.21±0.77	119.5±1.57	76.28±1.08

TABLE 3: DETERMINATION OF SERUM SELENIUM CONCENTRATION AND AGE ASSOCIATION IN TYPE-2 DIABETIC PATIENTS AND HEALTHY INDIVIDUALS

Age groups (years)	Diabetics' Serum Se Mean ± SEM (µg/L)	Healthy Serum Se Mean ± SEM (µg/L)	P value
20-38	548.07 ± 49.02	575.43 ± 30.12	0.641
39-56	576.31 ± 25.78	508.022 ± 25.81	0.070
57-75	615.32 ± 44.10	333.29 ± 22.69	0.000
	p=0.147	p=0.001	

TABLE 4: SERUM SELENIUM CONCENTRATIONS OF BOTH GROUPS WITH THEIR MINIMUM AND MAXIMUM VALUES

Groups		Mean ± SEM (µg/L)	Minimum (µg/L)	Maximum (µg/L)
Diabetics	Overall	580.64 ± 20.20	237.78	971.50
	Male	594.12 ± 29.29	300.43	937.50
	Female	569.92 ± 28.01	237.78	971.50
Healthy	Overall	536.38 ± 23.63	248.18	983.50
	Male	562.36 ± 27.56	263.25	983.50
	Female	475.78 ± 42.86	248.18	872.42

Type-2 diabetic patients were also grouped according to the duration of the disease into two subgroups: less than 5 years and equal to or more than 5 years. The mean serum selenium concentration of the former group was 540.80 ± 23.71 µg/L and of other group was 656.99 ± 32.81 µg/L.

There was a significant difference in the serum selenium concentration of smokers (640.77 ± 31.99

µg/L) and non-smokers (487.48 ± 26.94 µg/L) in the healthy group ($p<0.05$).

DISCUSSION: Serum selenium status influences various biological processes carried out in the body, such as thyroxine conversion, immunological reactions, and metabolic factors, *etc*. [11, 12, 13] Oxidative stress has an important role in the pathogenesis of vascular damage more profoundly observed in Type- 2 diabetes mellitus [14, 15].

Risk of development of diabetic complications is more in females than in men [16]. Selenium, being constituent of selenoproteins, plays an important role in the antioxidant defense system of the body. Hyperglycemia may influence absorption, distribution, and metabolism of selenium [10]. As the immune system becomes less efficient in the older age 17, a decrease in the serum selenium concentration may be an indicator of a decrease in antioxidant activity in healthy persons [11, 12].

Arnaud *et al.,* studied the serum selenium levels in French adults and showed that women had lower serum selenium concentration as compared to men. Decreased serum selenium was observed with the increased use of vegetables and fruit [18].

Safaralizadeh *et al.,* carried a study in Tehran on healthy individuals to determine the serum selenium concentration of the local population. They found that male adults had higher serum selenium concentration as compared to females [19]. Similarly, in our results, there existed a significant gender difference in the serum selenium levels of healthy individuals. This may be due to the dietary difference in the male and female population.

A study showed that the soil of Punjab is deficient in selenium content. Foods obtained from the plant source in Pakistan have low selenium content and foods obtained from animals and fish have high selenium content [20]. Pakistani population is a major consumer of animal-based diet [21], and its diet contains an adequate amount of selenium [22]. Therefore, the Pakistani population may have selenium content higher compared to other regions where a vegetarian diet is more common.

The mean selenium content determined by Usha *et al.,* [23] in India were 130.66 ± 37.18 µg/L and 51.9 ± 8.34 µg/L in healthy individuals and diabetic patients respectively, but our study showed that mean serum selenium in healthy subjects and diabetic patients were 530.40 ± 23.36 µg/L and 580.64 ± 20.20 µg/L respectively which are comparatively higher and showed no significant difference. More animal diet consumption in our population may be an explanation. A local study [24] showed mean blood selenium content to be 96 ± 3 µg/L. Variation in present results may be due to different analytical method.

Smoking decreases the immune function of the smoker, and resultantly oxidative stress is increased. Smoking is an additive metabolic risk factor in diabetes mellitus [25, 26]. Bleys *et al.,* [27] observed that there is a negative association between smoking and serum selenium concentration. However, in our study, there a positive association between smoking and serum selenium concentration as there was a significant difference in the serum selenium of smokers and non-smokers. The decrease in organification of selenium due to increased oxidative stress may be a reason.

Larijani *et al*., showed an insignificant difference in serum selenium of diabetic and non-diabetic subjects [28]. There was a borderline significant difference in the mean serum selenium levels of healthy and diabetic subjects in our study, leading us to conclude that serum selenium concentration may increase in diabetic patients. This may be due to the metabolic effect of hyperglycemia on the organification of Se in the body [27].

An Indian study showed a decrease in the selenium content of serum in diabetics as compared to healthy controls [23]. This study recommended selenium supplementation for the avoidance of diabetic complications, but we recommend caution in prescribing selenium supplementation for diabetic patients without consulting the baseline Selenium supplementation in elderly individuals with low selenium levels did not increase the risk of developing type 2 diabetes [29].

However, selenium supplementation should not be advocated in people with adequate selenium levels at baseline, as there have been some reports of increased diabetes risk with selenium supplementation [27, 30, 31].

CONCLUSION: The present study showed a marginally significant difference in the serum selenium levels between type 2 diabetic and healthy individuals. All the study participants had a replete selenium serum. Baseline laboratory investigations are of prime importance while prescribing selenium supplements in diabetic patients.

LIMITATIONS: A Sample size of our study was quite small, and there were many variables which could not be kept controlled. We strongly recommend further studies in our local population with large sample size and adjusted variables.

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CONFLICT OF INTEREST: Nil

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