SERUM SELENIUM LEVELS AMONG AIN SHAMS UNIVERSITY MEDICAL STUDENTS WITH FAMILY HISTORY OF CANCER, A PILOT STUDY

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ABSTRACT:

Background: *Previous researches showed that the level of distress experienced by family members especially first-degree relatives is higher than the one experienced by the patient himself. Selenium has been found to be associated with a reduced risk of all cancers at doses> 55 µg / day, The greatest positive anticancer mechanism of selenium may be contributed by the antioxidant function of GPxs and Selenoprotein P.*

Aim of the work: *The aim of this work is to compare serum levels of selenium in medical students who are first degree relatives of cancer patients to those with no family history of cancer.*

Patients and Methods: *This study is part of the Nutritional Assessment of Medical Students of Ain Shams University (NAMES-ASU) Project. Of the 1,200 medical students who came forward, 30 students were selected as the subject group (P) as they had a positive family history of cancer in first-degree relatives. The other 26 students were randomly selected from the rest of the sample with no family history of cancer to represent the control group (C). Selenium levels were measured from serum samples using Atomic Absorption Spectometry, stress was evaluated by a stress questionnaire and dietary Se intake was assessed using a food frequency questionnaire.*

Results: *The present study showed that the subject group had significantly higher stress levels than the control group (p = 0.003) with means of 13.92 and 18.27 for (C) group and (P) group respectively. Regarding stress and Se intake in relation to serum Se levels, they were statistically significant (p-Value 0.000 for both variables) However the Se dietary intake had more effect on serum Se levels than stress. The study also showed that age had an inverse relation to serum Se levels among both groups (p-Value was 0.021).*

Conclusion: *The Dietary Intake of Se, Stress and Age are significantly associated with serum Se levels. There is a negative correlation between Stress and Serum Selenium Levels.*

Key words: *Selenium, Cancer, Family History and Psychological Stress.*

INTRODUCTION:

According to the WHO, the global cancer burden raised up to 18.1 million new cases and 9.6 million deaths in 2018. The crude incidence rates on the national level for all sites excluding non-melanoma skin cancer in Egypt is 113.1/100,000 (both sexes), 115.7/100,000 (males), and 110.3/100,000 (females)[1].

A study estimated that 50 percent of certain types cancer can be preventable[2]. In addition, the World Cancer Research Fund estimates that about 20% of all cancers diagnosed in the US are related to several

preventable measures such as body fatness, physical inactivity, excess alcohol consumption as well as poor nutrition [3].

The psychological burden on family members of cancer patients especially first-degree relatives have been extensively studied in international literature. In fact, previous researches showed that the level of distress experienced by family members is higher than the one experienced by the patient himself[4&5].

Studies have shown that psychological stress increases circulating cytokines which in turn increases reactive oxygen species (ROS) that leads to increase in oxidative stress[6]. It has been estimated that around 1 billion people worldwide have inadequate selenium intake[7].

Selenium is present in many enzymes and proteins in their active centers, it has many roles such as activating anticancer agents, preventing heart and vascular diseases, exhibiting anti-proliferative and anti-inflammatory properties, and stimulating the immune system[8]. It also forms the main part of selenium-containing proteins and several antioxidant enzymes, such as glutathione peroxidase (GPx), thioredoxin reductase (TRxR), and iodothyronine deiodinase (DIO)[9].

The studies have shown that selenium may have anti carcinogenic effects, especially against cancers of the lung, prostate, skin, and GIT system [10]. Selenium resembles butyrate which induces DNA methylation and acts as an inhibitor of histone deactylase [11&12].

AIM OF THE WORK:

The aim of this work is to compare serum levels of selenium in medical students who are first degree relatives of cancer patients to those with no family history of cancer.

PATIENTS AND METHODS:

This study is part of the Nutritional Assessment of Medical Students of Ain Shams University (NAMES-ASU) Project which was designed to evaluate the nutritional status of the undergraduate medical students.

- -**Type of Study:** Comparable cross sectional study
- -**Study Setting:** Faculty of Medicine - Ain Shams University, Cairo, Egypt
- -**Study Period:** 3 months
- -**Target Population:** Medical students of Ain Shams University

Inclusion Criteria:

Cases included university students reporting positive first-degree family history of cancer

-Controls were selected randomly from university students without family history of cancer (neoplasms).

Exclusion Criteria for both cases and controls:

-Students on Selenium supplementation

-Students on Iron or Folic Acid supplementation

Sampling Method:

All students with positive family history of cancer in the first-degree relatives recruited from the nutritional survey project NAMES were invited to perform further testing to fulfill the aim of the current study. A total of 26 students without family history were randomly selected from the remain cohort reporting negative family history of neoplasm.

Study tools:

Further investigations were conducted on all medical students enrolled in the study and these included:

1. Detailed Nutritional questionnaire of Selenium intake (Mohamed et al, 2002)

2. Stress questionnaire (LAQ) (Craig et al., 1996, Tran et al., 2011): It includes questions regarding the general health and stress such as BMI, Coffee intake, smoking, exercise and meditation. The total possible score is 73. It's assumed that the higher the score the higher the stress level and higher risk of disease and lower quality of life.

3. Selenium measurement in plasma using Atomic Absorption Spectrometry at the National Research Center. Normal serum Se levels are 70-150 mcg/l. Below 70 considered low and above 150 considered high.

Ethical Considerations:

An informed written consent was obtained from each student before enrolment in the NAMES-ASU project explaining all benefits and risks and ensuring confidentiality.

Statistical analysis:

Recorded data were analyzed using the statistical Program (Minitab version 19). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following statistical tests were done:

Control and subject Groups we used One Way ANOVA for significance when comparing between the two means.

Regression was used for the Continuous independent variable or variables (Xs) in significance to a Continuous dependent variable (Y)

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the probability (p-value) was considered significant as the following:

- -P-value <0.05 was considered significant.
- -P-value <0.001 was considered as highly significant.
- -P-value >0.05 was considered insignificant.

RESULTS;

Of the 1,200 medical students who came forward, 56 were selected for analysis. More than 200 students had a positive family history of cancer, but only 30 students were selected as the subject group (P) because they had a positive family history of cancer in first-degree relatives, namely the mother and father. The other 26 students were randomly selected from the rest of the sample of students with no family history of cancer to represent the control group (C).

Table (1): Comparison between subjects and controls as regards stress using ANOVA (Analysis of Variance) test.

Source	DF	Adj SS	Adj MS	F-Value	P-Value
C/P	1	262.8	262.79	9.46	0.003*
Error	54	1499.7	27.77		
Total	55	1762.5			

*p-value>0.05 NS; *p-value <0.05 S; **p-value <0.001 HS*
SS : Sum of Squares, DF: Degree of Freedom, MS: Mean of Squares

Using the One Way ANOVA (Analysis Of Variance) to compare between the two groups in terms of stress levels, it showed the means were significantly different, the P-Value is 0.003 which states the significance. The Groups are responsible in interpreting 13.3% of the variability in the stress readings as shown in the graph above (table 1, fig.1).

Table (2): Comparison between the studied groups as regards selenium intake (mcg/l) and serum selenium (mcg/l) using ANOVA Test

EFFECT	SS	DF	MS	F	P- value
Selenium Intake					
C/P	21680.59	1	21680.59	18.53	0.000**
Residual	63186.84	54	1170.12		
Total	84867.43	55	1543.04		
C.V. (%): 44.08					
Serum Selenium					
C/P	1161.84	1	1161.84	22.81	0.000**
Residual	2750.55	54	50.94		
Total	3912.38	5	71.13		
C.V. (%): 12.36					

*p-value>0.05 NS; *p-value <0.05 S; **p-value <0.001 HS*

SS : Sum of Squares, DF: Degree of Freedom, MS: Mean of Squares

Tables 2 shows Comparison between control group and subject group as regards selenium intake and serum selenium levels. The above table shows statistical significance in selenium intake and serum selenium levels between subject group and control group.

Table (3): Regression Analysis of Serum Se (mcg/l) versus Stress and Se intake (mcg/l)

Source	DF	Adj SS	Adj MS	F-Value	P-Value
Regression	2	2167.9	1083.95	32.93	0.000
Stress	1	199.8	199.75	6.07	0.017*
Intake (mcg/l)	1	2167.4	2167.44	65.85	0.000**
Error	53	1744.5	32.91		
Total	55	3912.4			

*p-value>0.05 NS; *p-value <0.05 S; **p-value <0.001 HS*
SS : Sum of Squares, DF: Degree of Freedom, MS: Mean of Squares

We have two independent variables (Xs) (Stress & Intake (mcg/l) and one dependent variable (Y) Serum (mcg/l) by Using the Regression Analysis, we measured the effects of stress and Selenium intake (mcg/l) (Xs) on serum Selenium levels (mcg/l) (Y) between the two groups. The model explained 53.7% of the variability in the Y variable (Which means the two factors are responsible for the changes in the Serum (mcg/l) by 53.7%. The intake is influential than the stress as shown in the table above (Table 3).

In both groups the Age ranges from 18 to 25 with a median Age of 22 years.While the BMI ranges from 17 to 35 with a median BMI of 25. The Systolic Blood Pressure ranges from a minimum of 91 to a maximum of 148 with a median Systolic pressure of 112.5. And the Diastolic blood pressure has a minimum of 51 and maximum of 91 with a median Diastolic pressure of 71.5.

Analyzing the demographic factors of the two groups such as Age, BMI (Body Mass Index), Systolic blood pressure, Diastolic blood pressure, it was found that the BMI, Systolic blood pressure and Diastolic blood pressure were non significant with P-value of 0.326, 0.373, 0.352 respectively, While the Age was significant with P-value 0.021.

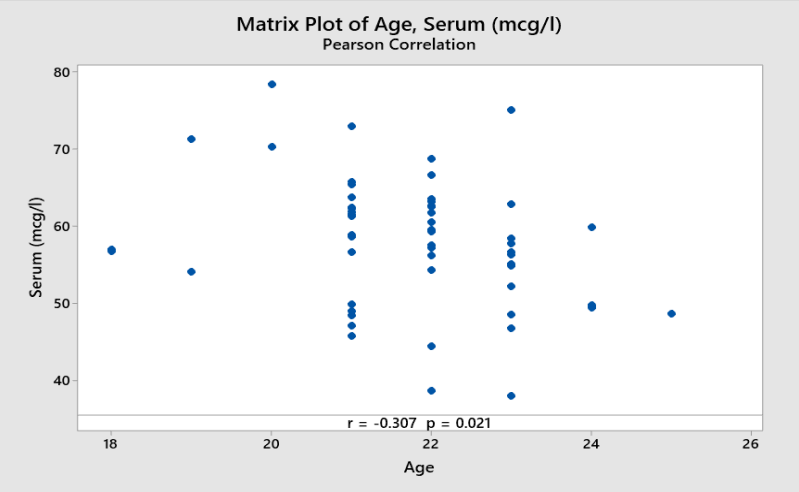

Diagram: Co-Relation between Age and Serum Se.

Using Pearson correlation for analysis of the relation between each of these variables (Age, BMI, Systolic and Diastolic blood pressure) and Serum Selenium level revealed that age is the only demographic factor that had an impact on Serum Selenium level with p-value of 0.021 as shown in diagram. This relation is an inverse relation meaning that the higher the age the lower the Serum Selenium level.

DISCUSSION;

Selenium deficiency has been estimated to be in around 1 billion people worldwide (Gerrad et al., 2017)[7]**.** Selenium is present in many enzymes, anti-oxidants and proteins in their active centers, it has many roles such as activating anticancer agents, preventing heart and vascular diseases, exhibiting anti-proliferative and anti-inflamatory properties, and stimulating the immune system (Duntas et al., 2015)[8].

This study was conducted to evaluate the effect of Stress on serum Se level in young medical students with positive family history of cancer.

Regarding Systolic and diastolic Blood Pressure in our study, they showed homogeneity (P-value of 0.373, 0.352 respectively). The systolic blood pressure mean was (114.24±14.02) and the diastolic blood pressure mean was (71.63±9.67). In present study, the BMI with a mean (25.20 ± 4.10) showed no statistical difference in the readings (P-value of 0.326) which means that subjects and control are homogeneous.

In current study, the Age with mean (21.75±1.42) was able to explain 7.7% from serum Se variance (statistically responsible for the variance, P-value < 0.005). In this point we are in line with Bizerea-Moga et al. (2021)**[15]** who conducted a retrospective observational cohort study, which evaluated serum Se status by age and gender in western Romania in which they found evidence of a correlation between serum Se concentration and population age. Also González-Estecha et al. (2016)[16], a study which found a correlation between serum selenium concentrations and age in an adult Spanish population, . This also coincide with Rasmussen et al. (2009)[17], study regarding Danish population.

On the other hand, our results differ with Burri et al. (2008)[18], study and Alehagen et al. (2016)[19] study were they found no correlation between Se concentrations and age in the general population. Different age ranges and characteristic dietary profiles as well as different health conditions of the sample

population may have triggered these discrepancies.

Regarding stress in this study, our results showed that the subject group had more stress levels than the control group. The two groups were significantly different (P-Value is 0.003), which is in alignment with Gerrad et al. (2017)[7]. In Turkey a descriptive study was done to identify the psychological symptoms and associated factors in adolescents who have a parent with cancer, it showed that a diagnosis of cancer in one of the parents had a devastating effect on the psychology of the children by causing stress, anxiety, fear, feelings of guilt, and agony which resulted in poor physical and psychological health and exhaustion.

Another Study by Huizinga et al. (2005)[20] were they studied Stress response symptoms in adolescent and young adult children of parents diagnosed with cancer showed that the rate of clinically elevated stress response symptoms was actually higher among the children of parents with cancer and the siblings of children treated for cancer than among children who had experienced cancer themselves.

In present study, we analyzed the stress and the dietary intake of Se in relation to the serum Se levels in both groups and we found that these two variables are explaining 53.7% of the variability in serum Se levels readings overall the population of the trial. However the Se dietary intake had more effect on serum Se levels than stress.

To the best of our knowledge this is the first study done to explore the correlation between Psychological Stress and Serum Selenium level. The generalizability of the results is limited by the small sample size and not analyzing the other variables in relation to serum Se as it would have been out of scope of this study and away from the aim. Due to COVID-19 Pandemic we weren't able to increase our demographic sample due to classes being switched to online to avoid over exposure of the students. This in turn caused another limitation in the study which is having a small demographic sample with a close range of age that may have not given us the opportunity to explore the full relationship between serum Se and age.

Conclusion:

In conclusion it was found that psychological stress had an inverse relation with serum Se. However daily Se intake from food had a much greater effect on serum Se level. Also age was found to have a significant association with lower values of serum Se in adolescents and young adults. The older students in both groups had lower serum Se levels than the younger ones did.

Recommendations:

We recommend for further research to be done with a bigger demographic sample and a wider age range. Also further research could study other correlations of Selenium with other factors.

REFERENCES:

1. Ibrahim SA., Khaled HM., Mikhail NH., Baraka H., et al. (2014). "Cancer Incidence in Egypt: Results of the National Population-Based Cancer Registry Program," Journal of Cancer Epidemiology, 2014: 18
2. Wolin, K.Y., Carson, K. & Colditz, G. A. (2010). Obesity and cancer. Oncologist, 15: 556.
3. Wcrf, A. (2014). Diet, nutrition, physical activity and prostate cancer., in Washington, DC: AIRC;. 2014.
4. Edwards, B. & Clarke, V. (2004). The psychological impact of cancer diagnosis on families: the influence of family functioning and patient's illness characteristics on depression and anxiety Psychooncology, 13: 562–576.
5. Segrin C, Badger T, Dorros SM, et al., (2007). Interdependent anxiety and

psychological distress in women with breast cancer and their partients. Psychooncology; 2007;16:634–643.

6. Teruo, H. (2014). Conversion of psychological stress into cellular stress response: Roles of the sigma-1 receptor in the process. Psychiatry and Clinical Neurosciences.
7. Gerrad D. Jones, Boris Droz, Peter Greve, et al.,(2017). Selenium deficiency risk predicted to increase under future climate change. Proceedings at the National Academy of Sciences of the United States of America; 2017; 114(11): 2848–2853.
8. Duntas, L.H. & Benvenga, S. (2015). Selenium: An element for life. Endocrine, 48: 756–775.
9. Kieliszek, M.; Błazejak, S.; Gientka, et al.(2015). Accumulation and metabolism of selenium by yeast cells. Appl. Microbiol. Biotechnol.; 2015, 99, 5373–5382
10. Lee, S.R., Bar-Noy, S., Kwon, J., et al. (2000). Mammalian thioredoxin reductase: Oxidation of the C-terminal cysteine/ selenocysteine active site forms a thioselenide, and replacement of selenium with sulfur markedly reduces catalytic activity. Proc Natl Acad Sci U S A, 97: 2521-2526.
11. Lee, J.I., Nian, H., Cooper, A.J.L., et al. (2009). α-Keto Acid Metabolites of Naturally Occurring Organoselenium Compounds as Inhibitors of Histone Deacetylase in Human Prostate Cancer Cells. Cancer Prev. Res, 2: 683–693.
12. Supic, G., Jagodic, M. & Magic, Z. (2013). Epigenetics: A New Link Between Nutrition and Cancer. Nutr. Cancer, 65: 781–792.
13. Mohamed et al,(2002). The Status Of Some Trace Elements In Some Egyptian Food Stuffs. Eucl.edu.eg;(http://srv5.eulc.edu.eg/eulc_v5/Libraries/Thesis/BrowseThesisPages.aspx?fn=ThesisPicBody&BibID=12289615&TotalNoOfRecord=32&PageNo=1&PageDirection=First)
14. Craig A, Hancock, K and Craig M.,(1996). The lifestyle appraisal questionnaire: A comprehensive assessment of health and stress, Psychology & Health; 1996;11(1): 331-343.
15. Bizerea-Moga, T. O., Pitulice, et al. (2021). Evaluation of Serum Selenium Status by Age and Gender: A Retrospective Observational Cohort Study in Western Romania. Nutrients; 13(5), 1497. https://doi.org/10.3390/nu13051497
16. González-Estecha, M., Palazón-Bru, I., Bodas-Pinedo, A., et al. (2017). Relationship between serum selenium, sociodemographic variables, other trace elements and lipid profile in an adult Spanish population. Journal of Trace Elements in Medicine and Biology, 43: 93–105.
17. Rasmussen, L. B., Hollenbach, B., Laurberg, P., et al. (2009). Serum selenium and selenoprotein P status in adult Danes – 8-year followup. Journal of Trace Elements in Medicine and Biology, 23(4): 265–271.
18. Burri, J., Haldimann, M. & Dudler, V. (2008). Selenium status of the Swiss population: Assessment and change over a decade. Journal of Trace Elements in Medicine and Biology, 22(2): 112–119.
19. Alehagen, U., Johansson, P., Björnstedt, M., et al. (2015). Relatively high mortality risk in elderly Swedish subjects with low selenium status. European Journal of Clinical Nutrition, 70(1): 91–96.
20. Huizinga, G. A., Visser, A., van der Graaf, W. T., et al. (2005). Stress response symptoms in adolescent and young adult children of parents diagnosed with cancer. European Journal of Cancer, 41(2): 288–295.

مستويات مصل السيلينيوم بين طلاب الطب بجامعة عين شمس مع تاريخ عائلي للسرطان ، دراسة تجريبية

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الخلفيه: أظهرت الأبحاث السابقة أن مستوى الضيق الذي يعاني منه أفراد الأسرة وخاصة الأقارب من الدرجة الأولى أعلى من المستوى الذي يعاني منه المريض نفسه. تم العثور على السيلينيوم مرتبطًا بانخفاض مخاطر الإصابة بجميع أنواع السرطان عند تناول جرعات أكبر من 55 ميكروغرام / يوم ، ويمكن أن تساهم وظيفة مضادات الأكسدة لـ GPxs و Selenoprotein P

الهدف: الهدف من هذا العمل هو مقارنة مستويات مصل السيلينيوم في طلاب الطب الذين هم أقارب من الدرجة الأولى لمرضى السرطان مع أولئك الذين ليس لديهم تاريخ عائلي للإصابة بالسرطان.

المرضى وطرق الدراسة: هذه الدراسة هي جزء من مشروع التقييم الغذائي لطلاب الطب بجامعة عين شمس (NAMES-ASU). من بين 1200 طالب طب تقدموا ، تم اختيار 30 طالبًا كمجموعة موضوعية (P) لأن لديهم تاريخًا عائليًا إيجابيًا للإصابة بالسرطان لدى أقارب من الدرجة الأولى. تم اختيار 26 طالبًا آخرين بشكل عشوائي من بقية العينة دون تاريخ عائلي للإصابة بالسرطان لتمثيل المجموعة الضابطة (C). تم قياس مستويات السيلينيوم من عينات المصل باستخدام مطياف الامتصاص الذري ، وتم تقييم الإجهاد عن طريق استبيان الإجهاد وتم تقييم المدخول الغذائي من Se باستخدام استبيان تردد الغذاء.

النتائج: أوضحت الدراسة الحالية أن المجموعة المستهدفة كانت لديها مستويات ضغط أعلى بكثير من المجموعة الضابطة (P = 0.003) بمتوسط 13.92 و 18.27 للمجموعة (C) و (P) على التوالي. فيما يتعلق بالإجهاد و Se المدخول فيما يتعلق بمستويات المصل Se ، كانت ذات دلالة إحصائية (قيمة p 0.000 لكلا المتغيرين) ومع ذلك ، فإن المدخول الغذائي من Se كان له تأثير أكبر على مستويات المصل أكثر من الإجهاد. كما أوضحت الدراسة أن للعمر علاقة عكسية بمستويات Se في المصل بين المجموعتين (قيمة p كانت 0.021).

الخلاصة: يرتبط المدخول الغذائي من Se والإجهاد والعمر بشكل كبير بمستويات المصل Se. هناك علاقة سلبية بين مستويات الإجهاد ومستويات السيلينيوم في الدم.

الكلمات الرئيسية: السيلينيوم والسرطان وتاريخ العائلة والضغط النفسي.