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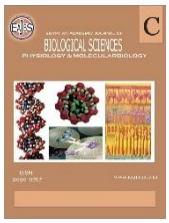

Association of Serum Selenium Levels and Insulin Resistance with Body Mass Index (BMI) in a Sample of Iraqi Individuals

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ABSTRACT

Selenium has recently been connected to insulin resistance (IR) and obesity due to its anti-inflammatory and anti-oxidant functions through selenoproteins. thus, the purpose of this study was to determine the relationship between BMI and serum selenium levels in participants with and without insulin resistance and to evaluate whether BMI is affected by selenium and insulin resistance status. (120) Iraqi (men and women) ranging between (18- 60) years old, with varying BMIs (normal weight, overweight, and obese) were included in a cross-sectional study. The Graphite Furnace Atomic Absorption Spectrophotometer was used to measure the serum level of selenium, and the ELISA technique was used to measure the fasting blood level of insulin. Among the 120 subjects, 25 (20.8%) were insulin resistant and 95 (79.2%) were non-insulin resistant. Insulin resistance was found in the group with significantly higher insulin than the non-insulin resistance group ($P<0.001$). Selenium levels significantly increased in the age group (31-50) years old but declined in the group of age > 50 years old ($P<0.001$). Selenium levels were significantly lower in females than males ($P=0.001$) and significantly decreased with increasing BMI ($P<0.001$). The findings revealed that serum selenium levels were linked to obesity, independent of insulin resistance.

INTRODUCTION

Minerals are essential to preserving general health. Enzymatic activation, preserving strong teeth and bones, controlling energy metabolism, boosting immunity, and supporting healthy muscle and brain function are all made possible by these microscopic chemical compounds. Millions of people worldwide suffer from mineral deficiencies brought on by insufficient or undernourished intake, with well-documented adverse health consequences of malnutrition. However, low mineral levels have also been linked to an increased risk of obesity and insulin resistance (IR) (Smita *et al.*,2022). Selenium is an essential mineral that has biochemical, molecular, and nutritional features. It participates in insulin metabolism and has anti-inflammatory and antioxidant properties that may help control insulin action signaling (Wongdokmai *et al* ., 2021). The presence of selenium (Se) in selenoproteins like glutathione peroxidase (GPx) and selenoprotein P (Sepp) is essential for human health as it performs a number of roles in normal health and metabolism. Selenium can be included in both organic (selenomethionine and selenocysteine) and inorganic (selenite and selenate) molecules (Genchi *et al* ., 2023).

The primary dietary sources of selenium include grains, dairy products, meat, fish, seafood, milk, and Brazil nuts. Rich sources of selenium include sea salt, eggs (only when fed in conjunction with selenium-containing yeast), giblets, bread, mushrooms, garlic, asparagus, and kohlrabi (enriched with this element). Selenium deficiency has been connected to myodegenerative diseases, cardiovascular disease, infertility, and cognitive decline (Shreenath *et al* ., 2023). Since 1975; excess body fat has been linked to overweight and obesity, which are serious health issues for the general public. Obesity has nearly tripled in prevalence worldwide, affecting people of all ages, genders, and socioeconomic, geographic, and ethnic backgrounds. presently, about one-third of the population suffers from excess obesity to some level (Chooi *et al* ., 2019). Excess adipose tissue contributes a major role in the etiology of other chronic diseases related to obesity by stimulating the production of oxidative stress and low-grade chronic inflammation. Recent studies have demonstrated the function of selenium in the regulation of important molecular pathways in the adipose tissue's physiology, including inflammation, oxidative stress, lipogenesis, and adipogenesis, the selenium nutritional status in overweight and obese people to assess whether the homeostasis of this element is altered by excess adiposity. Thus, either an excess or a deficiency of selenium can cause adipose tissue dysfunction and the consequent appearance of metabolic changes; this is especially significant when taking obesity into account (Fontenelle *et al* ., 2022). Dysregulation of insulin action and secretion, as well as enterocyte and adipocyte differentiation and function, have all been related to selenium, because it controls the expression of lipogenic enzymes, insulin signaling cascade enzymes, and hepatic carbohydrate metabolism. Adulthood is when the concentration of selenium reaches it,s maximum. In people over 60, the amount of this element in their serum is gradually declining (Tamari and Kim,1999). A deficiency of this element in the human body can be seen when its plasma concentration falls below 85 µg/L (Zwolak and Zaporowska,2012). Insulin resistance refers to the inability of insulin to promote glucose uptake by target tissue cells and the increased production of glucose by liver tissue. These factors result in the appearance of Hyperglycemia and hyperinsulinemia, which promotes the progression of type 2 diabetes mellitus (Freeman *et al.*, 2023). This study was conducted to investigate the relationship between BMI and serum selenium levels in participants with and without insulin resistance and to evaluate whether insulin resistance and selenium status have an impact on BMI.

MATERIALS AND METHODS

Study Design:

A cross-sectional study included (120)Iraqi individuals (male and female)in the age range between (18- 60) years old. lived in Baghdad city From (November 2022 to January 2023), these individuals were divided into three groups: included had to be in one of the following BMI categories: normal weight (BMI in the range of 18.5 to <25), overweight (BMI in the range of 25 to <30), and obese (BMI in the range of 30 or higher). Age and gender were matched in every group.

Sample Collection:

Five millilitres of venous blood were withdrawn from fasting participants (at least 8 hours fasting) in aseptic conditions using sterile simple tubes. It usually takes 10–20 minutes for the blood to clot when it is left undisturbed at room temperature (25-28) °C. After centrifuging the serum for 20 minutes at 3000 rpm, it was separated into tiny aliquots and stored at -20°C until further examination. Graphite furnace atomic absorption spectrophotometer (Shimadzu AA-7000 model) was used to measure serum selenium level, Fasting blood glucose was estimated by Spectrophotometer/ Microplate reader, while fasting blood insulin was measured by ELISA technique (sandwich enzyme immunoassay). The homeostasis model assessment was used

to measure IR (HOMA-IR) using the formula : (Fasting blood glucose (mg/dL) * Fasting blood insulin (µIU/ml)/ 405) (Kim *et al .,* 2021). The following equation was used to calculate the subject's BMI: body weight (kg) divided by height (m) squared. BMI = Weight (Kg)/Height2 (m2) (Tang *et al .,* 2022).

RESULTS

Table (1), presents the demographic characteristics of the study population. This table offers important information about the distribution of body mass index (BMI), sex composition, and age within the study population. The study participants' mean age was estimated to be 45 ± 10.29 years. Additionally, the median age, which was indicated as the central value of the age distribution, was found to be 30 years. The mean BMI of the study participants was calculated to be 31.5±5.35 (kg/m^2). The median BMI was found to be 27.45 (kg/m^2) and the range was 26.7 (kg/m^2). There were 56 (47.0%) male participants in the study and 64 (53.0%) female participants comprised the study's participant population.

Table 1: Demographic data of cases.

arameter			**Value**
Age (yr)	Mean±SD		45±10.29
	Median (Range)		30 (18-55)
Sex	Male	N (%)	56 (47.0)
	Female	N (%)	64 (53.0)
BMI (kg/m^2)	Mean±SD		31.5±5.35
	Median (Range)		27.45 (19.1-45.8)

The study participants' general characteristics were displayed in Table (2), among the 120 subjects, 25 (20.8%) were categorised as insulin resistant (IR) group and 95 (79.2 %) were characterised as non-insulin resistant (non-IR) group.

The IR group had a significantly higher insulin level than the non-IR group (p<0.001). Selenium levels were lower in the IR group than in the non-IR group, however, this decrease was insignificant. Age differences between the IR and non-IR groups were not statistically significant (p= 0.153). As well as the mean BMI was 28.28±1.11 (kg/m^2) for the IR group, in the non-IR group the mean BMI was 28.22±0.55 (kg/m^2) (p= 0.960) indicating that there was no statistically significant difference between the two groups. The two groups' fasting blood sugar levels did not differ significantly.

Table 2: Comparison of parameters between groups with IR and non-IR groups by unpaired t-test

Parameter	**Non-IR N=95 Mean±SE**	**IR N=25 Mean±SE**	**P value**
Age (yr)	33.07±1.09	29.76±1.75	0.153
BMI (kg/m^2)	28.22±0.55	28.28±1.11	0.960
Se (µg/I)	85.49±1.07	81.82±1.89	0.512
Insulin (µIU/ml)	3.84±0.22	27.78±2.77	**<0.001**
FBS (mg/dl)	72.47±0.91	73.16±2.4	0.789

The significance level is (p <0.05), and highly significant has the value (p<0.001). The cut-off value for insulin resistance is 2; any result above this suggests insulin resistance.

There was a statistically significant difference in the serum Se levels of the male and female participants, as revealed by

comparing the study's various parameters based on the participants' sex; female participants had lower mean Se levels (76.1±1.46 µg/l) than male participants (88.01±2.66 µg/l), (p = 0.001). Table (3), illustrates the significant difference that was noted in the IR and non-IR groups.

Table 3: Comparison of parameters according to sex in both groups (Insulin resistance and non-insulin resistance) by unpaired t-test**.**

Parameter	Sex	non-IR Mean±SE	P value	IR Mean±SE	P value
Age (yr)	Male	33.41±1.65	0.776	29.83±2.63	0.969
	Female	32.78±1.46		29.69±2.45	
BMI (kg/m^2)	Male	27.69±0.76	0.377	27.63±1.36	0.588
	Female	28.67±0.78		28.87±1.76	
Se (µg\ l)	Male	91.81±1.28	**<0.001**	88.01±2.66	**0.001**
	Female	80.04±1.22		76.1±1.46	
Insulin (µIU/ml)	Male	4.07±0.33	0.334	23.23±2.54	0.116
	Female	3.64±0.29		31.97±4.57	
FBS (mg/dl)	Male	72.45±1.47	0.978	75.18±2.86	0.432
	Female	72.5±1.15		71.31±3.83	

Non-IR group: Male = 44 and female =51, while IR group: Male =12 and female =13

In this study, in the non-IR group, we found a significant increase in serum selenium levels with age but declined in the group of age > 50 years old (p <0.001) when comparing the different parameters in this study according to age as shown in Table (4), in both groups.

Table 4: Comparison of parameters according to age in both groups (non-IR and IR groups)

Parameter	Age (yrs.)	Non-IR Mean±SE	P value*	IR Mean±SE	P value**
BMI (kg/m^2)	≤30	27.36±0.75	0.208	27.87±1.48	0.599
	31-50	28.63±0.87		29.15±1.55	
	>50	30.71±1.69		---	
Se (µg / l)	≤30	80.57±1.36	**<0.001**	79.32±1.91	0.052
	31-50	90.08±1.48		87.13±3.86	
	>50	87.87±3.57		---	
Insulin (µIU/ml)	≤30	4.03±0.3	0.676	27.04±3.24	0.706
	31-50	3.73±0.37		29.34±5.52	
	>50	3.4±0.49		---	
FBS (mg/dl)	≤30	72.12±1.38	0.462	70.99±3.03	0.192
	31-50	73.42±1.35		77.79±3.56	
	>50	69.33±2.82		---	

* P value by ANOVA, ** P value by unpaired t-test

Table (5), illustrates the highly significant decrease in serum selenium levels with increasing BMI that was observed in both groups when the various parameters in this study were compared based on BMI.

Table 5: Comparison of parameters according to body mass index in both groups (non-IR and IR) by ANOVA test**.**

Parameter	BMI (Kg/m^2)	Non-IR Mean±SE	P value*	IR Mean±SE	P value**
Age (yr)	Normal	31.63±1.89	0.695	22.4±2.98	0.075
	Overweight	34.15±1.69		30.46±2.35	
	Obese	33.73±1.99		33.71±3.16	
Se (µg/l)	Normal	94.32±1.32	**<0.001**	89.01±4.24	**0.003**
	Overweight	84.7±1.33		83.84±2.23	
	Obese	76.78±1.24		72.91±1.89	
Insulin (µIU/ml)	Normal	4.22±0.35	0.419	38.08±7.62	0.177
	Overweight	3.61±0.36		24.88±3.18	
	Obese	3.62±0.43		25.8±5.29	
FBG (mg/dl)	Normal	72.09±1.52	0.902	67.52±5.18	0.177
	Overweight	73.12±1.65		71.72±2.6	
	Obese	72.35±1.61		79.89±5.69	

Number of participants according to BMI (Normal=35, Overweight=27 and Obese=33 in the non-IR group, while Normal=5, Overweight=7 and Obese= 13 in IR group).

According to the receiver operating characteristic (ROC) curve; the area under the curve (AUC) for serum selenium levels selenium (Se) is 0.600, indicating that it is a moderate discriminator between individuals with insulin resistance vs. individuals without insulin resistance. Using a cutoff of 83.77(µg/l), it has a sensitivity of 54.7% and a specificity of 60.0%. These results are given in Figure (1) and Table (6).

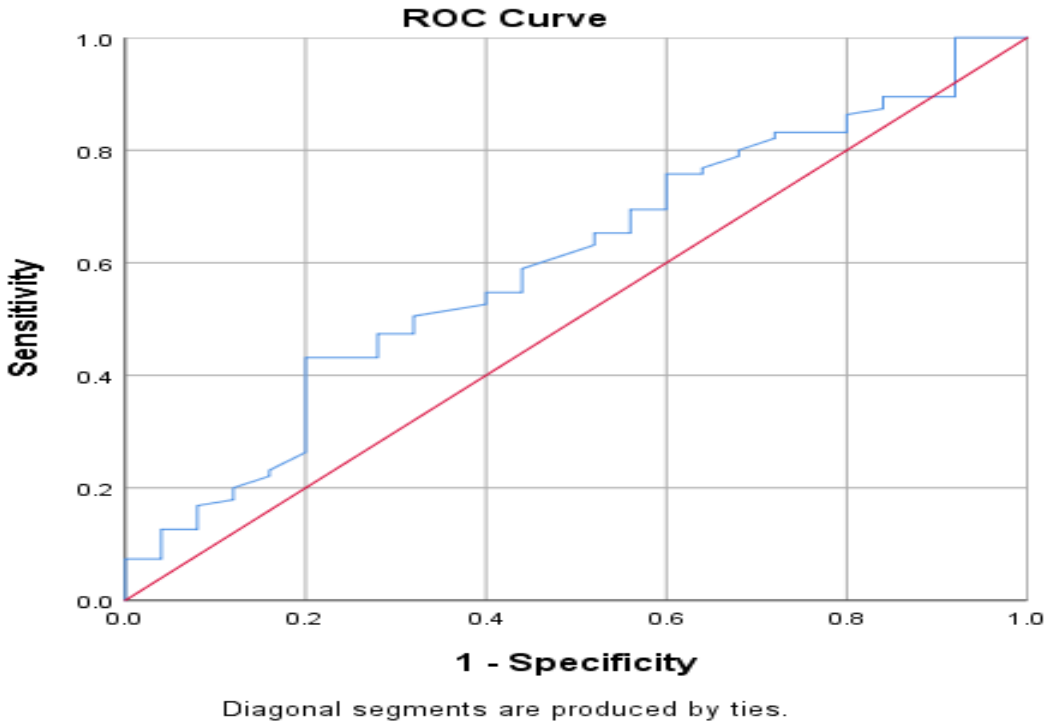

Fig. 1: ROC curve for selenium between IR and non-IR group**.**

Table 6: Area under the curve, sensitivity, specificity, and cutoff value of selenium between non-IR and IR groups

AUC	P value	Sensitivity	Specificity	Cutoff value
0.600	0.127	54.7%	60.0%	83.77(µg/l)

DISCUSSION

In this study, sex, age, and BMI were found to have statistically significant effects on differences in serum selenium levels; selenium levels were significantly lower in female participants than in male participants in both study groups (IR and non-IR). The main hypothesized causes of this discrepancy were sexual hormones and dietary variations; women tend to consume less selenium-rich foods than men. These results are in agreement with a number of other studies that found lower selenium levels in females when compared to male individuals (Kafai and Ganji, 2003, Safaralizadeh *et al* ., 2005). When compared to younger participants in this study, individuals in the age group (30-50) years had higher serum selenium levels, variations in selenium concentration across age groups may be brought on by changes in dietary choices, hormone status, environmental factors, and lifestyle (Sajjadi *et al* ., 2022, Letsiou *et al* ., 2014). There is evidence that older adults over 50 years old have significantly lower serum selenium levels, the relationship between aging and lower serum selenium levels is attributed to various factors, such as the build-up of inflammatory factors, physiological changes, insufficient consumption of selenium-rich foods, and inefficient absorption of dietary selenium (Sajjadi *et al* ., 2022, Bonaccors *et al* ., 2013). In relation to BMI; serum Selenium levels were significantly inversely related to BMI in both IR and non-IR groups, i.e., those in the normal weight group had the highest mean selenium levels, Subsequently, the group of overweight, individuals who were classified as obese with the lowest mean level of selenium. It is unclear what processes underlie the inverse relationships between serum selenium concentrations and BMI, however, they propose that the reduction of selenium in plasma or serum may be explained by the increased requirement for selenium to function as a cofactor of antioxidant protection enzymes in specific tissues resulting from the excessive production of reactive oxygen species in (obese, overweight) individuals. Studies have shown that the overproduction of pro-inflammatory cytokines by adipose tissue inhibits the synthesis of selenoproteins, such as SelP the main enzyme responsible for selenium transport in plasma, which may have a connection to chronic low-grade inflammation. This proposal aligned with previous studies (Tinkov *et al* ., 2020, Fontenelle *et al* ., 2021, Zhong *et al* ., 2018). The mechanisms underlying selenium and selenium protein metabolism interference in adipocyte physiology and obesity pathogenesis were discussed in these studies. It is possible that these mechanisms are primarily associated with controlling redox homeostasis and Endoplasmic reticulum stress (ERS). The hypothalamic management of satiety and eating habits is linked to the role of selenium in these mechanisms. In this study levels of serum selenium in participants with insulin resistance were deficient and lower than in participants without insulin resistance, the difference was not significant. Similar results were obtained from other studies (Gao *et al* ., 2014, Rios-Lugo *et al* ., 2022) while there are discrepancies with other studies (Pouresmaeil *et al* ., 2023, Casanova and Monleon, 2023). The accumulation of fat in other insulin-targeted tissues can also result from this dysfunction in obesity, which is characterized by hypertrophy and/or hyperplasia, it shows functional and structural alterations that influence the production and secretion pattern of pro-and anti-inflammatory adipocytokines, interfering with mechanisms involved in insulin action signaling pathways (Hajer *et al* ., 2008).

According to ROC curve investigation, the AUC for selenium is 0.600 indicating that there was a moderate

discrimination between individuals with insulin resistance vs. individuals without insulin resistance with the cutoff value of 83.77(µg/l). The main limitation of this study is a low sample size, especially the number of participants with insulin resistance being the group with the least number of participants.

Conclusion: In conclusion, serum levels of selenium were linked with obesity independent of insulin resistance. Selenium's effect could be due to an anti-oxidant/anti-inflammatory action. Further studies is required to validate our results and clarify the possible mechanisms.

Declarations:

Conflict of interests: The authors declare no conflict of interest.

Contributions:I hereby verify that all authors mentioned on the title page have made substantial contributions to the conception and design of the study, have thoroughly reviewed the manuscript, confirm the accuracy and authenticity of the data and its interpretation, and consent to its submission.

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REFERENCES

Bonaccorsi, G., Lorini, C., Bani Assad, G., Pepe, P., & Santomauro, F. (2013). Serum trace elements and risk of malnutrition in institutionalised elderly. *European journal of clinical nutrition*, 67(2), 155–160.

Casanova, P., & Monleon, D. (2023). Role of selenium in type 2 diabetes, insulin resistance and insulin secretion. *World journal of diabetes*, 14(3), 147–158.

Chooi, Y. C., Ding, C., & Magkos, F. (2019). The epidemiology of obesity. *Metabolism clinical and experimental*, 92, 6–10.

Fontenelle, L. C., Cardoso de Araújo, D. S., da Cunha Soares, T., Clímaco Cruz, K. J., Henriques, G. S., & Marreiro, D. D. N. (2022). Nutritional status of selenium in overweight and obesity: A systematic review and meta-analysis. *Clinical nutrition (Edinburgh, Scotland)*, 41(4), 862–884.

Fontenelle, L. C., Feitosa, M. M., Freitas, T. E. C., Severo, J. S., Morais, J. B. S., Henriques, G. S., Oliveira, F. E., Moita Neto, J. M., & Marreiro, D. D. N. (2021). Selenium status and its relationship with thyroid hormones in obese women. *Clinical nutrition ESPEN*, 41, 398–404.

Freeman, A. M., Acevedo, L. A., & Pennings, N. (2023). Insulin Resistance. In StatPearls. StatPearls Publishing.

Gao, H., Hägg, S., Sjögren, P., Lambert, P. C., Ingelsson, E., & van Dam, R. M. (2014). Serum selenium in relation to measures of glucose metabolism and incidence of Type 2 diabetes in an older Swedish population. *Diabetic medicine : a journal of the British Diabetic Association*, 31(7), 787–793.

Genchi, G., Lauria, G., Catalano, A., Sinicropi, M. S., & Carocci, A. (2023). Biological Activity of Selenium and Its Impact on Human Health. *International journal of molecular sciences*, 24(3), 2633.

Hajer, G. R., van Haeften, T. W., & Visseren, F. L. (2008). Adipose tissue dysfunction in obesity, diabetes, and vascular diseases. *European heart journal*, 29(24), 2959–2971.

Kafai, M. R., & Ganji, V. (2003). Sex, age, geographical location, smoking, and alcohol consumption influence serum selenium concentrations in the USA: third National Health and Nutrition Examination Survey, 1988-1994. *Journal of trace elements in medicine and*

biology : organ of the Society for Minerals and Trace Elements (GMS), 17(1), 13–18.

Kim, H. S., Cho, Y. K., Kim, E. H., Lee, M. J., Jung, C. H., Park, J. Y., Kim, H. K., & Lee, W. J. (2021). Triglyceride glucose-waist circumference is superior to the homeostasis model assessment of insulin resistance in identifying nonalcoholic fatty liver disease in healthy subjects. *Journal of clinical medicine*, 11(1), 41.

Letsiou, S., Nomikos, T., Panagiotakos, D. B., Pergantis, S. A., Fragopoulou, E., Pitsavos, C., Stefanadis, C., & Antonopoulou, S. (2014). Gender-specific distribution of selenium to serum selenoproteins: associations with total selenium levels, age, smoking, body mass index, and physical activity. *BioFactors (Oxford, England)*, 40 (5), 524–535.

Pouresmaeil, V., Al Abudi, A. H., Mahimid, A. H., Sarafraz Yazdi, M., & Es-Haghi, A. (2023). Evaluation of serum selenium and copper levels with inflammatory cytokines and indices of oxidative stress in type 2 diabetes. *Biological trace element research*, 201(2), 617–626.

Rios-Lugo, María Judith, Ana Gabriela Palos-Lucio, Claudia Inés Victoria-Campos, Angel Lugo-Trampe, Karina Del Carmen Trujillo-Murillo, Maximiliano Arahon López-García, Marisol Espinoza-Ruiz, Elizabeth Teresita Romero-Guzmán, Héctor Hernández-Mendoza, and Consuelo Chang-Rueda. 2022. "Sex-Specific association between fasting plasma glucose and serum selenium levels in adults from Southern Mexico" *Healthcare*, 10, no. 9: 1665

Safaralizadeh, R., Kardar, G. A., Pourpak, Z., Moin, M., Zare, A., & Teimourian, S. (2005). Serum concentration of selenium in healthy individuals living in Tehran. *Nutrition journal*, 4, 32.

Sajjadi, S. S., Foshati, S., Haddadian-Khouzani, S., & Rouhani, M. H. (2022). The role of selenium in depression: a systematic review and meta-analysis of human observational and interventional studies. *Scientific reports*, 12(1), 1045.

Shreenath, A. P., Hashmi, M. F., & Dooley, J. (2023). Selenium Deficiency. In StatPearls. Stat Pearls Publishing.

Smita, R. M., Shuvo, A. P. R., Raihan, S., Jahan, R., Simin, F. A., Rahman, A., Biswas, S., Salem, L., & Sagor, M. A. T. (2022). The role of mineral deficiencies in insulin resistance and obesity. *Current diabetes reviews*, 18(7), e171121197987.

Tamari, Y., & Kim, E. S. (1999). Longitudinal study of the dietary selenium intake of exclusively breast-fed infants during early lactation in Korea and Japan. *Journal of trace elements in medicine and biology : organ of the Society for Minerals and Trace Elements (GMS)*, 13(3), 129–133.

Tang, N., Ma, J., Tao, R., Chen, Z., Yang, Y., He, Q., Lv, Y., Lan, Z., & Zhou, J. (2022). The effects of the interaction between BMI and dyslipidemia on hypertension in adults. *Scientific reports*, 12(1), 927.

Tinkov, A. A., Ajsuvakova, O. P., Filippini, T., Zhou, J. C., Lei, X. G., Gatiatulina, E. R., Michalke, B., Skalnaya, M. G., Vinceti, M., Aschner, M., & Skalny, A. V. (2020). Selenium and

selenoproteins in adipose tissue physiology and obesity. *Biomolecules*, 10(4), 658.

Wongdokmai, R., Shantavasinkul, P. C., Chanprasertyothin, S., Panpunuan, P., Matchariyakul, D., Sritara, P., & Sirivarasai, J. (2021). The involvement of selenium in type 2 diabetes development related to obesity and low grade inflammation. *Diabetes, metabolic syndrome and obesity : targets and therapy*, 14, 1669–1680.

Zhong, Q., Lin, R., & Nong, Q. (2018). Adiposity and Serum Selenium in U.S. adults. *Nutrients*, 10(6), 727.

Zwolak, I., & Zaporowska, H. (2012). Selenium interactions and toxicity: a review. Selenium interactions and toxicity. *Cell biology and toxicology*, 28(1), 31–46.