Research Article

INTERNATIONAL RESEARCH JOURNAL OF PHARMACY

www.irjponline.com

ISSN 2230-8407 [LINKING]

EVALUATING THE RELATIONSHIP BETWEEN GLYOXALASE 1 AND SERUM LEVELS OF MAGNESIUM, MANGANESE AND SELENIUM IN INDIVIDUALS WITH DIABETES MELLITUS

Dr Krishan Bihari Verma,[1] Dr Rajendra Singh Paviaya,[2] Dr Dharmveer Sharma,[3] Dr Rashmi Tomar[4*]

[1]MBBS MD, Professor, Department of Physiology, SRVS Medical College, Shivpuri, Madhya Pradesh
[2]MBBS MD, Assistant Professor, Department of Physiology, SRVS Medical College Shivpuri, Madhya Pradesh
[3]MSc, PhD, Associate Professor, Department of Biochemistry SRVS Medical College Shivpuri MP
[4*]MBBS MD, Associate Professor, Department of Microbiology, SRVS Medical College Shivpuri, Madhya Pradesh

Address for Correspondence
Dr Rashmi Tomar
Email id: drrashmitomar797@gmail.com

How to cite: Verma KB, Paviaya RS, Sharma D, Tomar R. Evaluating the relationship between glyoxalase 1 and serum levels of magnesium, manganese and selenium in individuals with diabetes mellitus. International Research Journal Of Pharmacy, 2023,14:9:1-5. Doi: 10.56802/2230-8407.1303701

ABSTRACT

Background: Glyoxalase-1 is an erythrocyte enzyme that is part of the glyoxalase system. It aids in the catabolization of methylglyoxal and is also a precursor for AGEs (advanced glycation end products). Elevated levels of AGEs and methylglyoxal result in diabetic complications that are impacted by Glyoxalase levels.

Aim: The objective of this study was to assess the levels of serum magnesium (Mg), manganese (Mn), and selenium (Se) in different groups defined by the length of diabetes mellitus.

Methods: The present study 252 participants with diabetes mellitus between the ages of 30 and 70 were evaluated and compared the concentration of different micronutrients, namely manganese, selenium, and magnesium. For biochemical investigations, the level of Glycated haemoglobin (GlyHb) was measured for each subject with lipid levels. An entirely automated analyzer and the immunoturbidity enhance enzymatic (IEE) approach were used to analyse glycated haemoglobin. ELISA was used to measure the levels of Glyoxalase-1. One-way ANOVA, the independent t-test, and the chi-square test were used in the statistical analysis of the collected data.

Results: glyoxalase-1 levels were strongly correlated with glycated haemoglobin, selenium, and magnesium levels (p-values of 0.007, 0.02, and <0.001, respectively), whereas manganese levels were not significantly correlated (p=0.72).

In diabetic patients, glyoxalase-1 is a good predictor of inadequate glycemic control. In diabetic people, there is a correlation between high levels of glycoxalase and the premature onset of problems. Serum magnesium, selenium, and manganese concentrations all show a decline as diabetes duration increases.

Results: Groups I and II had mean diabetes durations of 2.22±0.94 years and 6.83±1.92 years, similar mean BMIs (24.3±3.1 and 23.6±3.5 kg/m2, p=0.74), Glycated haemoglobin for laboratory studies was 8.9±2.3 and 9.9±2.5 (p=0.02) respectively. the levels of triglycerides, total cholesterol, HDL (high-density lipoproteins), LDL (low-density lipoproteins), and VLDL (very low-density lipoproteins) were similar in both groups. Glyoxalase-1 levels were strongly correlated with glycated haemoglobin, selenium, and magnesium levels (p-values of 0.007, 0.02, and <0.001, respectively), whereas manganese levels were not significantly correlated (p=0.72).

Keywords: Advanced glycation end products, Diabetic complications, Methylglyoxal, Micronutrients, Nephropathy, Neuropathy, Retinopathy

INTRODUCTION

Diabetes mellitus is a metabolic illness that affects a lot of people worldwide, and it is becoming more common in India. For healthcare professionals, diabetes mellitus is a worry since, during the course of its course and longevity, it is linked to a variety of macro and micro problems as well as organ damage. In addition to being essential for lipid metabolism, antioxidant enzymes, glucose homeostasis, and possible pro-oxidant catalysts, micronutrients play a critical role in these processes.[1] There is a direct or indirect connection between certain micronutrients and diabetes problems. Glyoxalase-1 and the erythrocytic enzyme of the glyoxalase system catabolize methylglyoxal. Furthermore, the primary precursor of AGEs is methylglyoxal. Diabetes problems have a close correlation with elevated levels of AGEs and methylglyoxal.[2] Magnesium deficiency is typically observed in individuals with diabetes, with incidence rates ranging from 11% to 48%. The development of diabetic complications is impacted by magnesium deficiency in patients with diabetes mellitus, which is also associated with altered lipid metabolism and insulin resistance.[3]

Selenium (Se) has a role in lowering the peroxidase production of free radicals and lipoproteins, which are seen in lower concentrations in diabetic people and are associated with a higher risk of heart problems from diabetes mellitus. Manganese (Mn) is also essential for the development and progression of diabetes mellitus and its related problems.[4] Studies in the past have compared the amounts of micronutrients in persons with diabetes mellitus and in those in good health. Nevertheless, there is a paucity of information in the literature about the comparison of magnesium, selenium, and manganese levels in individuals with diabetes mellitus.[5] The literature search illustrated below revealed that relatively few research have evaluated the relationship between glyoxalase-1 and trace elements, specifically Mn, Se, and Mg, in individuals with diabetes mellitus.[6]

Thus, the current study set out to evaluate magnesium, manganese, and selenium concentrations in individuals with diabetes mellitus and compare them with other groups based on different groups depending on the length of diabetes mellitus. The study connected the micronutrient assessments with the levels of glyoxalase-1 in individuals with diabetes mellitus.

MATERIALS AND METHODS

The current prospective cross-sectional clinical investigation sought to determine the levels of magnesium, manganese, and selenium in participants with diabetes mellitus and to compare those levels with those of other groups based on distinct groupings based on the duration of diabetes mellitus. The study also evaluated the levels of glyoxalase-1 in subjects with diabetes mellitus and was correlated with the micronutrients assessed. The study was carried out at Department of Physiology, SRVS Medical College, Shivpuri, Madhya Pradesh. Subjects from the institute's outpatient section made up the research population.

252 participants with diabetes mellitus between the ages of 30 and 70 were evaluated for the study. The participants were split into two groups: Group I had diabetes for less than four years, while Group II had diabetes for more than four years. The glyoxalase-1 level and serum trace element levels were used to construct the groups based on the short- and long-term consequences of diabetes. The research excluded participants who met any of the following criteria: they had to be pregnant, nursing, or on micronutrients, hormone therapy, hepatic carcinoma, anaemia, obesity, thyroid dysfunction, liver diseases, chronic renal disease (apart from nephropathy), or both. After finally including the subjects in the study, verbal and written informed consent was taken.

Following inclusion, a thorough medical history was taken for each participant, along with sociodemographic information about age, gender, and social habits. Clinical information was obtained, including blood pressure measurements, BMI, the length of the patient's diabetes, and family history. Diabetic complications, such as neuropathy, nephropathy, and retinopathy, were evaluated and compared between the two groups to determine the effect of the length of the patient's diabetes on the complications. For biochemical investigations, the level of Glycated haemoglobin (GlyHb) was measured for each subject with lipid levels. After an 8-hour fast, 5 millilitres of blood was drawn from the antecubital vein.

Following plasma separation, the acquired sample was diluted using glycerol. To determine the concentration of Se, Mn, and Mg in the serum, an auto spectrometer was used. The trace element concentrations in the serum were evaluated using the calibration curve. An entirely automated analyzer and the immunoturbidity enhance enzymatic (IEE) approach were used to analyse glycated haemoglobin. ELISA was used to measure the levels of Glyoxalase-1 in 5 millilitres of drawn blood samples that were placed in a disposable, non-endotoxin tube and left to clot for two hours at room temperature. Following clotting, the sample was centrifuged for 15 minutes at 2 to 8 degrees Celsius, and the supernatant was used in an ELISA.

One-way ANOVA, the independent t-test, and the chi-square test were used in the statistical analysis of the collected data. The data were expressed in mean ± standard deviation (SD). The significance level was assessed at $p<0.05$. SPSS software version 22.0 was used for data analysis.

RESULTS

252 participants with diabetes mellitus between the ages of 30 and 70 were evaluated for the study. The participants were split into two groups: Group I had diabetes for less than four years, while Group II had diabetes for more than four years. Group II had a substantially greater mean age of study individuals (58.64±4.77 years) than Group I (49.34±7.52 years) with a p-value of less than 0.001. Group I had 60.9% (n=78) men, whereas Group II had 61.3% (n=76) males. In Groups I and II, there were 39.1% (n=50) and 38.7% (n=48) females, respectively. With p=0.53, the gender distribution in the two groups was comparable. In two groups, the participants who smoked and drank alcohol were similar (p=0.13 and 0.23, respectively). In 12.5% of the individuals (n = 16) and 21% of the subjects (n = 26), the family history of diabetes was positive (p = 0.13). Dyslipidemia subjects were similar across the two groups (p=0.42). Groups I and II had mean diabetes durations of 2.22±0.94 years and 6.83±1.92 years, respectively (Table 1).

Group I and II patients had similar mean BMIs (24.3±3.1 and 23.6±3.5 kg/m2, respectively; p=0.74). With p<0.001, group II participants had considerably higher diastolic and systolic blood pressures than group I subjects. Glycated haemoglobin for laboratory studies was 9.9±2.5 in Group II and 8.9±2.3 in Group I (p=0.02). As indicated by Table 1, however, the levels of triglycerides, total cholesterol, HDL (high-density lipoproteins), LDL (low-density lipoproteins), and VLDL (very low-density lipoproteins) were similar in group I and II participants with p=0.86, 0.75, 0.77, 0.44, and 0.85, respectively.

Glyoxalase-1 and trace element levels were evaluated across the two study groups, and the results showed that group II had considerably higher selenium levels than group I (52.26±5.42 ng/dL and 78.97±16.57 ng/dL, respectively, with p<0.001). Group I had considerably greater manganese levels (0.223±0.36 mg/dL) than Group II (0187±0.016 mg/dL; p<0.001). Group I had considerably higher magnesium levels than Group II, measuring 1.687±0.334 and 1.344±0.166 mcg/L, respectively, with a p-value of less than 0.001. Table 2 shows that the levels of glyoxalase in Group II were substantially higher at 50.63±5.34 ng/mL with p<0.001 than in Group I at 41.27±3.56 ng/mL.

Regarding evaluating the relationship between study groups' levels of Glyoxalase-1, glycated haemoglobin, and trace elements Table 3 indicates that glyoxalase-1 levels were strongly correlated with glycated haemoglobin, selenium, and magnesium levels (p-values of 0.007, 0.02, and <0.001, respectively), whereas manganese levels were not significantly correlated (p=0.72).

DISCUSSION

Regarding the research subjects' demographics, Group II had a mean age of 58.64±4.77 years, which was substantially higher than Group I's mean age of 49.34±7.52 years (p<0.001). There were 60.9% (n=78) males in Group I and 61.3% (n=76) males in Group II. There were 39.1% (n=50) and 38.7% 9n=48) females in Groups I and II respectively. With p=0.53, the gender distribution in the two groups was comparable. In two groups, the participants who smoked and drank alcohol were similar (p=0.13 and 0.23, respectively). In 12.5% of the individuals (n = 16) and 21% of the subjects (n = 26), the family history of diabetes was positive (p = 0.13). Dyslipidemia subjects were similar across the two groups (p=0.42). Groups I and II had mean diabetes durations of 2.22±0.94 years and 6.83±1.92 years, respectively. These clinical traits and patients' demographics aligned with those evaluated by Makhlough A et al.[7] (2015) and Patke V et al.[8] (2015), who evaluated subjects with similar demographics to the current investigation.

Group I and II patients' BMIs in the current research were comparable, at 24.3±3.1 and 23.6±3.5 kg/m2, respectively, with a p-value of 0.74. With p<0.001, group II participants had considerably higher diastolic and systolic blood pressures than group I subjects. Glycated haemoglobin for laboratory studies was 9.9±2.5 in Group II and 8.9±2.3 in Group I (p=0.02). Nonetheless, group I and II participants had similar levels of triglycerides, total cholesterol, HDL (high-density lipoproteins), LDL (low-density lipoproteins), and VLDL (very low-density lipoproteins) (p=0.86, 0.75, 0.77, 0.44, and 0.85, respectively). The laboratory parameters evaluated in the investigations by Eva H et al.[9] in 2017 and Riaz M et al.[10] in 2014 were equivalent to the laboratory data used in this investigation.

When glyoxalase-1 and trace elements were examined across the two study groups, it was observed that group II had considerably greater selenium levels than group I, with 52.26±5.42 ng/dL and 78.97±16.57 ng/dL, respectively, with p<0.001. Group I had considerably greater manganese levels (0.223±0.36 mg/dL) than Group II (0187±0.016 mg/dL; p<0.001). Group I had considerably higher magnesium levels than Group II, measuring 1.687±0.334 and 1.344±0.166 mcg/L, respectively, with a p-value of less than 0.001. Group II had considerably greater glyoxalase levels (50.63±5.34 ng/mL) than Group I (41.27±3.56 ng/mL; p<0.001). The current study's findings were in line with those of Sanjeevi N et

al.[11] (2018) and Mohammed RR et al.[12] (2018), who found that diabetics had comparable levels of magnesium, manganese, and selenium.

Glycated haemoglobin, selenium, and magnesium levels were significantly correlated with glyoxalase-1 levels, with corresponding p-values of 0.007, 0.02, and <0.001, respectively, for the assessment of the association between glyoxalase-1 levels, glycated haemoglobin, and trace elements in study groups. In contrast, manganese showed a non-significant correlation with glyoxalase-1 levels, with p=0.72. The present study's results were consistent with earlier research conducted by Kumar P et al.[13] (2019) and Nigro C et al.[14] (2017), which found a substantial correlation between glyoxalase-1 and blood levels of magnesium, selenium, and glycated haemoglobin.

The primary findings of the research indicated that glyoxalase-1 levels rose as the duration of diabetes increased, whereas Mn, Se, and Mg concentrations declined and may be linked to problems from diabetes. Moreover, there is a strong correlation observed in diabetic people between their glyoxalase levels and their Mn and Se levels. Elevated glyoxalase-1 levels have been linked to elevated glycated haemoglobin levels. According to these results, glyoxalase-1 levels may serve as a good predictor of the onset of diabetic problems early in life, poor glycemic control in diabetic people, and a correlation between the ageing process of diabetes and magnesium and selenium shortage. These results were consistent with earlier research by Shamsaldeen YA et al.[15] (2016) and Malam PP et al.[16] (2016), which also revealed comparable outcomes.

CONCLUSION

The current study shows, taking limitations into account, that Glyoxalase-1 is a good predictor of poor glycemic control in diabetes individuals. In diabetic individuals, high levels of the enzyme glutathione are linked to the early development of problems. Serum magnesium, selenium, and manganese concentrations all show a decline as diabetes duration increases.

REFERENCES

1. Laclaustra M, Navas-Acien A, Stranges S, Ordovas JM, Guallar E. Serum selenium concentrations and diabetes in US adults: National Health and Nutrition Examination Survey (NHANES) 2003–2004. Environ Health Persp 2009;117:1409-13.
2. Geiger H, Wanner C. Magnesium in disease. Clin Kidney J 2012;5:25–38.
3. Rabbani N, Thornalley PJ. The critical role of methylglyoxal and glyoxalase 1 in diabetic nephropathy. Diabetes 2014;63:50-2.
4. Abou-Seif MA, Youssef AA. Evaluation of some biochemical changes in diabetic patients. Clinica Chimica Acta 2004;346:161-70
5. Wang X, Zhang M, Lui G, Chang H, Zhang M, Liu W, et al. Associations of serum manganese levels with prediabetes and diabetes among ≥60-year-old Chinese adults: a population-based cross-sectional analysis. Nutrients 2016;8:497.
6. Wahid A, Verma GC, Meena CP, Pathan AR. Study of serum magnesium level in patients with type 2 diabetes mellitus and its correlation with glycosylated Haemoglobin and diabetic complications. Int J Adv Med 2017;23:2.
7. Makhlough A, Makhlough M, Shokrzadeh M, Mohammadian M, Sedighi O, Faghihan M. Comparing the levels of trace elements in patients with diabetic nephropathy and healthy individuals. Nephro-urology 2015;7:28576.
8. Patke V, Saroj S. Erythrocyte enzymes of Glyoxalase system as indicators of beneficial effects of antihyperglycemic agents in Type 2 Diabetes. Int J Res Med Sci 2015;3:1650.
9. Eva H, Akhter QS, Alam MK, Ahmed S. Serum chromium and selenium levels in type 2 diabetes mellitus. J Bangladesh Soc Physiol 2017;12:72-5.
10. Riaz M, Mahmood KT, Irfan K. Serum levels of selenium in uncomplicated type-2 diabetic patients and healthy individuals. Int J Pharma Sci Res 2014;5:4219.
11. Sanjeevi N, Freeland-Graves J, Beretvas SN, Sachdev PK. Trace element status in type 2 diabetes: A meta-analysis. J Clin Diag Res 2018;12:01.
12. Mohammed RR, Mehrez MM, Abdel-Maksoud H. Biochemical relations between copper, selenium, zinc, and magnesium with the glycemic state of diabetic pregnant women. Benha Med J 2018;35:344.
13. Kumar P, Bhargava S, Agarwal PK, Garg A, Khosla A. Association of serum magnesium with type 2 diabetes mellitus and diabetic retinopathy. J Family Med Pri Care 2019;8:1671.
14. Nigro C, Leone A, Raciti GA, Longo M, Mirra P, Formisano P, et al. Methylglyoxal-glyoxalase 1 balance: the root of vascular damage. Int J Mol Sci 2017;18:188.

15. Shamsaldeen YA, Mackenzie LS, Lione LA, Benham CD. Methylglyoxal, A Metabolite Increased in Diabetes is Associated with Insulin Resistance, Vascular Dysfunction and Neuropathies. Curr Drug Metab 2016;17:359–67.
16. Malam PP, Amin AJ, Zala AC, Navadiya VM, Patel D, Patel DA. Study of oxidative stress parameters in type-II diabetes mellitus and their correlation with blood glucose level. Int J Curr Res Rev 2016;8:31.

TABLES

Characteristics	**Group I (≤4 years) (n=128) % (n)**	**Group II (>4 years) (n=124) % (n)**	**p-value**
Mean age (years)	49.34±7.52	58.64±4.77	**<0.001**
Clinical history			
Diabetes (family history)	23.4 (30)	17.7 (22)	0.26
Dyslipidemia	78.1 (100)	80.6 (100)	0.42
Social habits			
Alcohol	12.5 (16)	21 (26)	0.13
Smoking	42.2 (54)	33.9 (42)	0.23
Gender			
Males	60.9 (78)	61.3 (76)	0.53
Females	39.1 (50)	38.7 (48)	
Diabetes duration (years)	2.22±0.94	6.83±1.92	-
BMI (kg/m2)	24.3±3.1	23.6±3.5	0.74
Blood pressure			
Systolic	123.6±6.4	128.5±6.6	**<0.001**
Diastolic	82.6±3.6	85.5±3.5	**<0.001**
Laboratory investigations			
VLDL	43.8±10.1	43.5±9.6	0.86
LDL	94.2±22.3	92.7±20.6	0.75
HDL	42.4±5.7	41.7±6.5	0.77
Triglycerides	220.2±44.7	227.1±50.6	0.44
Total cholesterol	195.8±22.7	196.8±27.4	0.85
GlyHb	8.9±2.3	9.9±2.5	**0.02**
Diabetic complications			
Nephropathy	3.1 (4)	16.1 (20)	
Retinopathy	4.7 (6)	24.2 (30)	
Neuropathy	10.9 (14)	37.1 (46)	**<0.001**

Table 1: Clinical and socio-demographic characteristics of two study groups with diabetes

Enzymes and elements	**Group I (≤4 years) (n=128)**	**Group II (>4 years) (n=124)**	**p-value**
Selenium (ng/dL)	78.97±16.57	52.26±5.42	**<0.001**
Manganese (mg/dL)	0.223±0.36	0.187±0.016	**<0.001**
Magnesium (mcg/L)	1.687±0.334	1.344±0.166	**<0.001**
Glyoxalase-1 (ng/mL)	41.27±3.56	50.63±5.34	**<0.001**

Table 2: Intergroup comparison of glyoxalase-1 and trace elements in two study groups

Enzymes and elements	**f-value**	**p-value**
Glycated hemoglobin	1.986	**0.007**
Manganese	0.87	0.72
Selenium	1.736	**0.02**
Magnesium	3.583	**<0.001**

Table 3: Association of Glyoxalase-1 levels, glycated hemoglobin, and trace elements in study groups