Research Article

INTERNATIONAL RESEARCH JOURNAL OF PHARMACY

www.irjponline.com

ISSN 2230-8407 [LINKING]

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

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How to cite: Godbole C, Godbole S. Evaluating the relationship between Glyoxalase 1 and Blood Levels of Magnesium, Manganese, and Selenium in individuals with Diabetes Mellitus. International Research Journal Of Pharmacy, 2010,1:1:441-446.

Accepted: 12/10/2010, published: 02/12/2010

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ABSTRACT

Background: First of all, Glyoxalase-1 is an erythrocyte enzyme that is part of the glyoxalase system and aids in the catabolization of methylglyoxal. Additionally, AGEs (advanced glycation end products) are precursors to this enzyme. Glyoxalase levels affect the development of diabetes problems caused by elevated AGE and methylglyoxal levels. There is little information on the relationship between trace elements and glyoxalase-1 in diabetics.

Aim: The current investigation set out to assess blood levels of magnesium (Mg), manganese (Mn), and selenium (Se) in different groups based on how long each group had had diabetes mellitus.

Methods: In order to correlate the concentration of micronutrients with glyoxalase-1 levels, the current study compared the concentration of several micronutrients, specifically manganese, selenium, and magnesium, in two groups: Group I was non-complicated and had diabetes duration of ≤4 years, and Group II had complications and diabetes duration of > 4 years. There were a total of 252 subjects with diabetes in this group.

Results: Group II had considerably greater levels of selenium and glyoxalase-1 (52.26±5.42 ng/dL and 78.97±16.57 ng/dL, respectively, with $p<0.001$) than group I. Group I had considerably greater amounts of manganese and magnesium ($p<0.001$) than Group II. Glycated hemoglobin, selenium, and magnesium levels in study groups were shown to be substantially correlated with glyoxalase-1 levels, with p-values of 0.007, 0.02, and less than 0.001, respectively, whereas, manganese showed a non-significant association with glyoxalase-1 levels with $p=0.72$.

Conclusion: In individuals with diabetes, glyoxalase-1 is a good indicator 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.

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 (advanced glycation end products) 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 to those of other 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. The study was conducted after approval from the relevant Institute ethical committee. Subjects from the institute's outpatient section made up the research population.

The study evaluated 252 participants with diabetes mellitus who ranged in age from 30 to 70 years old and had different times of start. The participants were split into two groups. Subjects in Group I had diabetes for less than four years, whereas those in Group II had the disease 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, anemia, obesity, thyroid dysfunction, liver diseases, chronic renal disease (apart from nephropathy), or both. Once the participants in the research were eventually included, informed permission was obtained both verbally and in writing.

Following inclusion, a thorough medical history was taken of each participant, and sociodemographic information about age, gender, and social habits was also documented. Systolic and diastolic blood pressure, body mass index (BMI), length of diabetes, and family history were the clinical data collected. To determine the effect of the length of diabetes on the problems, the diabetic complications, such as retinopathy, neuropathy, and nephropathy, were evaluated and compared in the two groups. Glycated hemoglobin (GlyHb) levels were measured for biochemical analyses in all participants with lipid levels.

After an 8-hour fast, 5 ml of blood was drawn under sterile circumstances from the antecubital vein. Serum was then extracted from the blood sample and frozen at -80oC. The centrifugation process took 10 minutes at 4000 rpm. 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 assess glycated hemoglobin. ELISA was used to measure the levels of Glyoxalase-1 in 5 milliliters 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.

The data gathered were analyzed statistically using the chi-square test and independent t-test along with one-way ANOVA. 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). The family history of diabetes was positive in 12.5% (n=16) and 21% (n=26) subjects respectively (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 hemoglobin 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.

Glycated hemoglobin, selenium, and magnesium levels were significantly correlated with glyoxalase-1 levels, with corresponding p-values of 0.007, 0.02, and <0.001, respectively, when the association between glyoxalase-1 levels, glycated hemoglobin, and trace elements was evaluated in study groups. Manganese, on the other hand, showed a non-significant correlation with glyoxalase-1 levels, with p=0.72, as indicated in Table 3.

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 mean age of 49.34±7.52 years ($p<0.001$). 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. These clinical traits and patients' demographics aligned with those evaluated by Makhlough A et al. (2015) and Patke V et al. (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 hemoglobin 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 McLellan AC et al[7] and Beisswenger PJ et al[8] 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 Ahmed N et al[9] and Ruggenenti P et al,[10] who found that diabetics had comparable levels of magnesium, manganese, and selenium.

Glycated hemoglobin, 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 hemoglobin, 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 Beisswenger PJ et al[11] and Yao D et al,[12] which found a substantial correlation between glyoxalase-1 and blood levels of magnesium, selenium, and glycated hemoglobin.

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. Increased levels of glycated hemoglobin have been associated with increased levels of glyoxalase-1. 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 aging process of diabetes and magnesium and selenium shortage. These results were consistent with earlier research by Duran-Jimenez B et al[13] and Dobler D et al,[14] 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.

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TABLES

S. No	Characteristics	Group I (≤4 years) (n=128) % (n)	Group II (>4 years) (n=124) % (n)	p-value
1.	**Mean age (years)**	49.34±7.52	58.64±4.77	**<0.001**
2.	**Clinical history**			
a)	Diabetes (family history)	23.4 (30)	17.7 (22)	0.26
b)	Dyslipidemia	78.1 (100)	80.6 (100)	0.42
3.	**Social habits**			
a)	Alcohol	12.5 (16)	21 (26)	0.13
b)	Smoking	42.2 (54)	33.9 (42)	0.23
4.	**Gender**			
a)	Males	60.9 (78)	61.3 (76)	0.53
b)	Females	39.1 (50)	38.7 (48)	
5.	**Diabetes duration (years)**	2.22±0.94	6.83±1.92	-
6.	**BMI (kg/m2)**	24.3±3.1	23.6±3.5	0.74
7.	**Blood pressure**			
a)	Systolic	123.6±6.4	128.5±6.6	**<0.001**
b)	Diastolic	82.6±3.6	85.5±3.5	**<0.001**
8.	**Laboratory investigations**			
a)	VLDL	43.8±10.1	43.5±9.6	0.86
b)	LDL	94.2±22.3	92.7±20.6	0.75
c)	HDL	42.4±5.7	41.7±6.5	0.77
d)	Triglycerides	220.2±44.7	227.1±50.6	0.44
e)	Total cholesterol	195.8±22.7	196.8±27.4	0.85
f)	GlyHb	8.9±2.3	9.9±2.5	**0.02**
9.	**Diabetic complications**			
a)	Nephropathy	3.1 (4)	16.1 (20)	
b)	Retinopathy	4.7 (6)	24.2 (30)	
c)	Neuropathy	10.9 (14)	37.1 (46)	**<0.001**

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

S. No	Enzymes and elements	Group I (≤4 years) (n=128)	Group II (>4 years) (n=124)	p-value
1.	**Selenium (ng/dL)**	78.97±16.57	52.26±5.42	**<0.001**
2.	**Manganese (mg/dL)**	0.223±0.36	0.187±0.016	**<0.001**
3.	**Magnesium (mcg/L)**	1.687±0.334	1.344±0.166	**<0.001**
4.	**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

S. No	Enzymes and elements	f-value	p-value
1.	**Glycated hemoglobin**	1.986	**0.007**
2.	**Manganese**	0.87	0.72
3.	**Selenium**	1.736	**0.02**
4.	**Magnesium**	3.583	**<0.001**

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