DOI:https://doi.org/10.53350/pjmhs2023177207

ORIGINAL ARTICLE

Correlation of serum Omentin-1 levels with Diabetic peripheral neuropathy in Type-2 diabetes mellitus patients

MUHAMMAD SAMEER HANIF[1], AMINA NADEEM[2], TALLAT NAUREEN[3], KAMIL ASGHAR IMAM[4], SIDRA ASLAM[5], MUHAMMAD KALEEM[6]

[1]*Assistant Professor, Department of Physiology, Poonch Medical College, Rawalakot, AJ&K Pakistan*
[2]*Professor, Department of Physiology, Army Medical College/ National University of Medical Sciences (NUMS), Rawalpindi Pakistan*
[3]*Assistant Professor, Department of Physiology, Army Medical College/ National University of Medical Sciences (NUMS), Rawalpindi Pakistan*
[4]*Associate Professor, Department of Physiology, Army Medical College/ National University of Medical Sciences (NUMS), Rawalpindi Pakistan*
[5]*Assistant Professor, Department of Pathology, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur, AJ&K Pakistan*
[6]*Assistant Professor, Department of Pathology, Divisional Headquarters Teaching Hospital, Mirpur, AJ&K Pakistan*
Correspondence to: Muhammad Sameer Hanif, Email: dctrsameer@gmail.com

ABSTRACT

Objective: To establish correlation of serum omentin-I with diabetic peripheral neuropathy in type-2 diabetes mellitus (T2DM).

Methods: The study was conducted at the Physiology Department, Army Medical College in collaboration with Pak Emirates Military Hospital, Rawalpindi from January 2019 to December 2019. Total 90 participants were recruited by non-probability purposive technique and were divided into three groups of 30 each. Group-I, Group-II and group-III consisted of healthy, T2DM individuals without diabetic peripheral neuropathy (DPN) and T2DM participants with DPN respectively. DPN was assessed by Michigan Neuropathy Screening Instrument (MNSI). Serum omentin-I levels were determined by enzyme-linked immunosorbent assay (ELISA).

Results: Fasting blood glucose (FBG) levels and glycated hemoglobin (HbA1c) were considerably lower in group-I as compared to in group-II and group-III. There was a significant difference of body mass index (BMI) between the groups, but the difference between group-I and group-II as well as between group-II and group-III was not significant. There was observed a statistically significant difference of mean serum omentin-1 levels within all three groups with p-value < 0.0001 with highest levels in Group-I and lowest in Group-III. Serum omentin-I levels were negatively correlated with T2DM, T2DM induced DPN, HbA1c, BSF and BMI.

Conclusion: Serum omentin-I is an anti-inflammatory & anti-oxidant adipocytokine in T2DM and has potential protective beneficial role in preventing DPN.

Keywords: Omentin-1, Diabetic peripheral neuropathy, Type-2 diabetes mellitus

INTRODUCTION

Type 2 diabetes mellitus is a pandemic health problem causing decreased life span, quality and economic problems for individuals and nations. It is a disease of imbalance in metabolism of carbohydrates, lipids and proteins due to defective use / action and/or relative decreased secretion of insulin leading to chronic high blood sugar levels. The pathogenesis of T2DM includes insulin resistance and later on dysfunction of insulin production after chronic increased production initially, which lead to the dysregulation of the blood sugar levels.[1] Globally five million deaths are attributable to T2DM and it has been forecasted that T2DM will affect almost 642 million population of the world between the ages of 20 and 79 years.[2]

The most frequently occurring complication of diabetes, which is present in one third to one half of the patients with T2DM, is diabetic peripheral neuropathy (DPN). DPN is characterized by impairment in the functioning of peripheral nerves and it is mostly present in lower extremities especially the feet but it can also disturb the nerves of upper extremities.[3] Reduced, bizarre or loss of sensation is the dominant symptom of DPN in which distal portions of the nerves of lower extremities are mostly involved. Numbness, pickling or pain sensations in the lower extremities are also frequent symptoms. Individuals with DPN can have serious consequences for the quality of life.[4]

Omentin-1, an adipocytokine, which is secreted and expressed by cells of vascular stroma in adipose tissues of viscera's.[5] Multiple researches have revealed that omentin-1 is more influential in the prognosis of T2DM than subcutaneous obesity.[6] Circulating omentin-1 is a protective factor as it exerts anti-inflammatory (by suppressing tumor necrosis factor) as well as anti-oxidant effects against hyperglycemia induced progression of T2DM and its complications.[7]

We wanted to assess and establish correlation of omentin-1 with peripheral neuropathy induced by T2DM as there is a very little data available about the levels of omentin-1 in relation to diabetes induced peripheral neuropathy as well as omentin-1 levels in Pakistani healthy and diabetic population.

Received on 15-01-2023
Accepted on 25-06-2023

MATERIAL AND METHODS

It was a cross sectional case control study conducted at Physiology department and Centre for Research in Experimental and Applied Medicine (CREAM) Laboratory Army Medical College, Rawalpindi in collaboration with the Pak Emirates Military Hospital, Rawalpindi from January 2019 to December 2019. After the formal approval from Ethical Review Committee of Army Medical College a sample of 90 was taken and it was divided into three groups having sample size of 30 each. Non- probability purposive sampling technique was applied to select the study participants.

Thirty healthy individuals of either gender were included in the Group-I (Control group). Thirty individuals of either gender with T2DM diagnosed within 5 years without DPN were included in Group-II (Case-I group). Thirty individuals of either gender having T2DM along with DPN were included in the Group-III (Case-II group). Individuals with Type-1 Diabetes mellitus, non-diabetic causes of neuropathy, pregnancy, autoimmune disease, infectious disease, renal or pulmonary or hepatic or cardiac disease, tumour or those using anti-inflammatory medications in the preceding six to eight weeks were not included in the study as well as those not consenting to participate.

All the participants undertook an informed and written consent in English and Urdu as well as their bio-data, demographic data and medical history relevant to our study was noted on a written proforma. A systemic clinical examination was followed by recording of vital signs for all the subjects. Controls were selected from the individuals coming for regular health check-ups and recently diagnosed T2DM patients were recruited from medical OPD of PEMH, Rawalpindi.

Height (meters) and weight (kilograms) of all the participants was measured for BMI calculation and peripheral neuropathy was assessed by using Michigan Neuropathy Screening Instrument (MNSI).[8] MNSI had two components, one was patient's self-assessment questionnaire filled by patient and the other

component was for physical assessment of both feet of all the participants performed by the researcher.[9] A modified version of MNSI was used which excluded monofilament testing from the physical assessment.[10] The history questionnaire was a 15-item self-administered questionnaire, responses of "yes" to all items except 7 and 13 was considered as a single point whereas for 7 and 13 "no" response was considered as single point. Scoring criteria was removed from questionnaire to waive prejudice. Points ≥4 were regarded positive for peripheral neuropathy. Physical assessment of each foot included inspection, presence or absence of ulceration, assessing the sense of vibration together with ankle reflexes by the researcher. Score was given to each of the findings with minimum o and maximum 4 score for each foot. A score of ≥1 was considered abnormal and positive for peripheral neuropathy. A combined scoring approach of MNSI patient version and MNSI health care profession component for labelling DPN showed sensitivity of 95.4% when results were compared with gold standard nerve conduction study.[11]

Strict aseptic measures were taken as per protocol to draw blood for the biochemical parameters assessment. 5 ml of blood sample was taken and relocated to gel separator tube and centrifugation was done by setting the speed at 2000-3000 rpm for a period of 20 minutes at room temperature. Pipetted serum was shifted to the polypropylene tubes and stored at -20^{0}C. Fasting blood glucose levels were assessed by using glucometer (ACCU CHEK). For the measurement of Glycated haemoglobin (HbA1c) in blood samples, ADVIA -1800 instrument by Siemen was used. Serum Omentin-1 quantitative levels were measured by using Human Omentin-1 ELISA Kit (Glory Science Company Limited, USA having Catalog No SKU: 11629). The detection range was 3.3pg/ml - 200 pg/ ml for omentin-1. Sandwitch ELISA methodology was applied in the procedure as omentin-1 specific antibody had already been coated in micro ELISA plate. Stat Fax 2100 microplate ELISA reader was set at 450 nm wavelength, and prompt determination of OD value of all the wells was done after completing all the steps of ELISA. A standard curve was plotted with OD values at 450 nm on the y-axis and standard concentration (pg/ml) on the x-axis and the quantitative omentin-1 levels were noted for all the samples.

Presentations of results for quantitative variables were taken as mean and standard deviation. One way analysis of variance (ANOVA) and Post-Hoc Tukey's test was utilised for the comparison of variables in all the three groups. Pearson correlation coefficients determined correlation between the three groups. Statistical package for social sciences (SPSS) version 22 was utilized for statistical analysis and *p*-value was regarded as significant if it was ≤ 0.05.

RESULTS

Our 90 study participants were divided into the three groups with thirty individuals each and having fifteen male and female participants in each group. Group-I had non-diabetic healthy individuals as controls and their mean age was 40 ± 11.35 (years). Group II consisted of newly diagnosed T2DM patients without DPN as cases-I with the mean age 46.53 ± 10.97 (years). Group III included diagnosed cases of T2DM with DPN as cases-2 with mean age 52.68 ± 8.59 (years).

BMI was highest in group III (27.92 ± 3.04) than group II (26.51 ± 2.82) and group I (24.98 ± 2.97). The difference between all of the three groups was significant at *p*-value 0.001. There was an insignificant difference amid group I and group II at *p*-value 0.119 and a significance difference between group I and group III at *p*-value was 0.001. There was no significant difference in mean BMI values within group II and group III as their *p*-value was 0.156.

BSF mean value was significantly higher in group II (166.76 ± 47.37) and group III (176.56 ± 70.79) in comparison to group I (89.66 ± 5.64) with *p*-value of 0.0001. The difference among the groups was significant at *p*-value < 0.0001. There was a significant difference of BSF levels at *p*-value < 0.0001 of group I with group II and III and there was no significant difference within group II and group III, as their *p*-value was 0.722.

The mean value of HbA1c was significantly lower in group I (5.06 ± 0.35) as compared to that of group II (8.58 ± 1.53) and group III (9.37 ± 1.94). HbA1c was significantly higher in group II along with III in comparison with group I and the difference across the groups was significant with *p*-value < 0.0001. Significant difference of mean HbA1c levels at *p*-value < 0.0001 of group I with group II and III was observed and an insignificant difference within group II and group III, as their *p*-value was 0.092.

Omentin-1 levels were spotted to be significantly different in all the three groups at *p*-value < 0.0001. The mean values of Omentin-1 were found to be highest in Group I (1235.33 ± 127.56) in comparison to Group II (787.33 ± 141.39) and Group III (288.66 ± 140.7). The mean values of Omentin-1 were detected to be significantly high in Group II as compared to Group III with *p*-value < 0.0001 (Figure 1).

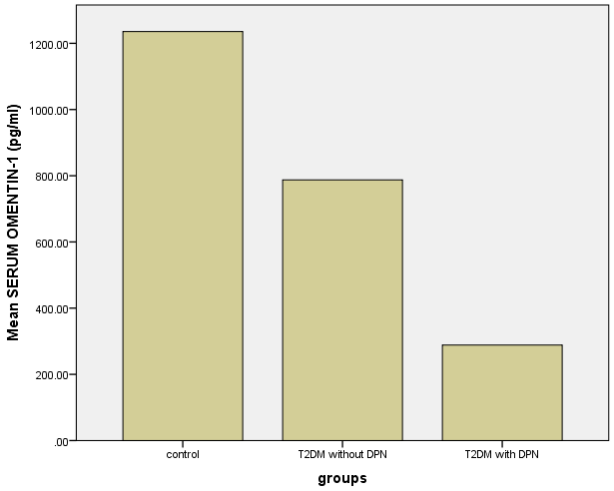

Figure 1: Mean values of serum Omentin-1 across three groups where group I (control), group II (T2DM without DPN) and group III (T2DM with DPN) are graphically represented by bar- chart and values of all the groups are statistically different from each other after one way ANOVA with *p*-value < 0.0001.

Correlation bivariate analysis exhibited that levels of Omentin-1 in serum were negatively correlated with BMI as weak correlation , with BSF as moderate correlation and with HbA1c as strong correlation (Table-1).

Table 1: Correlation of serum Omentin-1 levels with other parameters

Parameter	Parameters being correlated	*r*- value	*p*-value
Serum Omentin-1	BMI	-0.320	0.002*
	BSF	-0.517	<0.0001*
	HbA1c	-0.698	< .0001*

Correlation is significant at the 0.01 level. There is significant negative correlation of serum omentin-1 with BMI, BSF and HbA1c. (n=90)

DISCUSSION

T2DM has emerged as a universal public health issue and owing to modern digital sedentary lifestyle involving people of all ages its incidence and prevalence is increasing to an epidemic level. Asia has more than 60% of diabetes cases out of the total global cases.[12] An estimation of 150% rise of type 2 diabetes mellitus cases has been anticipated in South Asia between 2000 and 2035.[13] In Pakistan the prevalence of T2DM and pre-diabetes is 16.98% and 10.91% respectively which is much higher and alarming public health issue than previously thought.[14] The most common diabetic complication affecting up to half of diabetic patients is DPN and it is the major culprit causing disability due to

foot ulceration and amputation. Increased Health costs related to diabetes and low quality of life is attributable to this micro-vascular complication of T2DM.[15]

We evaluated, for the first time in Pakistan, the correlation of omentin-1 levels in serum with diabetic peripheral neuropathy in type-II diabetes mellitus patients. There was a significant difference in mean BMI values within group I and group III of our study. This significant BMI difference among groups is backed by a study that validates the association of higher BMI with higher risk of diabetes related complications.[16]

In our study the fasting blood glucose levels in group II and III in comparison with group I were found to be significantly high. Past studies validate these results because ineffective glucose consumption mechanisms and resultant hyperglycemia leads to the development of T2DM and its complications.[17]

In our study higher levels of HbA1c were indicated in group II and III than in group I. These findings were consistent with literature and previous studies which revealed that higher levels of HbA1c being linked particularly with the chronic hyperglycemia as well as development of T2DM induced complications.[18]

Results of omentin-1 in healthy and T2DM individuals in our study are consistent with the findings of previous studies which revealed lower omentin-1 levels in T2DM group than non-diabetic group implying that omentin-1 has an insulin sensitizing role and its lack is a contributory factor in advancement of resistance to insulin actions.[19]

Our study results are consistent with a study which was conducted to assess the serum and vitreous levels of omentin-1 in diabetic microvascular complication retinopathy. This study had four groups including healthy group, diabetic retinopathy (DR) group, NPDR group and PDR group. PDR patients depicted significantly reduced levels of omentin-1 in serum and vitreous in comparison with other three groups.[20]

Recently a study revealed findings that there was a negative correlation between omentin-1 levels in serum with the existence and severe form of DR in T2DM and their findings were consistent with our study findings that omentin-1 levels are negatively correlated with T2DM induced microvascular complications like DPN, DR and DN.[21]

Similar results as our study were observed in a study that evaluated the omentin-1 levels in patients of T2DM with and without T2DM induced diabetic nephropathy (DN). They divided study participants into equal groups of 41 with DN and without DN as cases and controls group respectively. They noted significant decreased omentin-1 levels and deduced significant role of inflammatory pathways as well as insulin resistance mechanisms in pathophysiology of DN in T2DM as anti-inflammatory, anti-oxidant and insulin sensitizing adipocytokine like omentin-1 levels are reduced in DN.[22]

Association of omentin-1 levels with insulin resistance in chronic kidney disease patients has shown that levels of omentin-1 in serum are associated negatively with insulin resistance as well as in chronic kidney disease caused by T2DM. These results are in conjunction with our study results which revealed negative correlation of omentin-1 with T2DM and its induced DPN.[23]

Serum omentin-1 levels were negatively correlated with rising BSF and HbA1c levels by moderate and high correlation. HbA1c levels are usually high in those T2DM patients who have poor control on their diabetes so this signifies the role of uncontrolled diabetes in development of T2DM induced microvascular complications like DPN. Our this finding is in consistent with the finding of a study that omentin-1 has significant negative correlation with HbAlc levels in T2DM induced diabetic retinopathy implying role of uncontrolled T2DM and high HbA1c role in development of T2DM induced microvascular complications like DR, DPN and DN.[24]

Serum omentin-1 levels in our study were significantly lower in individuals with T2DM induced DPN as compared T2DM and healthy subjects implying a negative correlation between T2DM induced DPN and circulatory omentin-1 levels. A case-control study was carried out and 40 participants were allocated in four groups. First group having diabetic foot syndrome (DFS), second having diabetic subjects without DFS, third having non-diabetics with foot lesions and fourth having non-diabetic subjects. DFS subjects showed significant lower concentrations of serum omentin-1 levels as compared to other groups. Result of this recent study is consistent with our results in which the omentin-1 circulatory serum levels are lowest in the group of DPN.[25]

We can deduce from our study that omentin-1 is a beneficial adipocytokine owing to its insulin sensitizing as well as anti-inflammatory role. Circulatory omentin-1 levels are reduced in T2DM and its complications so it can be used as a diagnostic and prognostic marker for T2DM and its complications. In future this anti-inflammatory marker may be used as a therapeutic target for prevalent diseases like T2DM to prevent, reverse or slow onset of T2DM and its debilitating and fatal complications.

CONCLUSION

Serum omentin-I levels reduce insulin resistance implying that decreasing levels has a possible causative role in development of insulin resistance in T2DM. Serum omentin-I levels has beneficial role in diabetic peripheral neuropathy in T2DM patients.

Disclaimer: None.
Conflict of interest: None.
Funding disclosure: HEC, Pakistan.

REFERENCES

1. Xu W, Owens D & Weng J. 2018. Short-Term Intensive Insulin Therapy in Patients with Newly Presenting Type 2 Diabetes. Endocrine and Metabolic Medical Emergencies: A Clinician's Guide. 548-559.
2. Ogurtsova K, Da Rocha Fernandes J, Huang Y, Linnenkamp U, Guariguata L, Cho N, Cavan D, Shaw J & Makaroff L. 2017. IDF Diabetes Atlas: Global estimates for the prevalence of diabetes for 2015 and 2040. Diabetes research and clinical practice. 128: 40-50.
3. Papanas N & Ziegler D. 2015a. Risk factors and comorbidities in diabetic neuropathy: an update 2015. The review of diabetic studies: RDS. 12(1-2): 48.
4. Gylfadottir S S, Weeracharoenkul D & Andersen S T. 2019. Painful and non-painful diabetic polyneuropathy: Clinical characteristics and diagnostic issues. 10(5): 1148-1157.
5. Schoettl T, Fischer I P & Ussar S. 2018. Heterogeneity of adipose tissue in development and metabolic function. Journal of Experimental Biology. 221(Suppl 1): jeb162958.
6. Buyukinan M, Atar M, Can U, Pirgon O, Guzelant A & Deniz I. 2018. The association between serum vaspin and omentin-1 levels in obese children with metabolic syndrome. Metabolic syndrome and related disorders. 16(2): 76-81.
7. Zhou J-Y, Chan L & Zhou S-W. 2014. Omentin: linking metabolic syndrome and cardiovascular disease. Current vascular pharmacology. 12(1): 136-143.
8. Feldman E L, Stevens M J, Thomas P K, Brown M B, Canal N & Greene D A. 1994. A practical two-step quantitative clinical and electrophysiological assessment for the diagnosis and staging of diabetic neuropathy. Diabetes Care. 17(11): 1281-9.
9. Moghtaderi A, Bakhshipour A & Rashidi H. 2006. Validation of Michigan neuropathy screening instrument for diabetic peripheral neuropathy. Clinical neurology and neurosurgery. 108(5): 477-481.
10. Pabellano-Tiongson M L G, Javelosa G F J & Tan A D A. 2019. Validity of the Filipino Version of the Michigan Neuropathy Screening Instrument as a Measure of Distal Symmetric Peripheral Neuropathy among Diabetic Patients in the Clinic. Asian Journal of Research and Reports in Neurology. 1.9.
11. Dagang D J, Diestro J D, Hamoy-Jimenez G, Isip-Tan I T & Reyes J P B. 2016. Validation of the Filipino-Translated Version of the Michigan Neuropathy Screening Instrument among Filipino Patients with Diabetes Mellitus Seen at the Philippine General Hospital. Journal of the ASEAN Federation of Endocrine Societies. 31(2): 115.
12. Zostautiene I, Jorde R, Schirmer H, Mathiesen E B, Njølstad I, Løchen M-L, Wilsgaard T, Joakimsen R M & Kamycheva E. 2015. Genetic variations in the Vitamin D receptor predict type 2 diabetes and myocardial infarction in a community-based population: the Tromsø study. PloS one. 10(12).
13. Nanditha A, Ma R C, Ramachandran A, Snehalatha C, Chan J C, Chia K S, Shaw J E & Zimmet P Z. 2016. Diabetes in Asia and the

Pacific: Implications for the Global Epidemic. Diabetes Care. 39(3): 472-85.
14. Aamir A H, Ul-Haq Z, Mahar S A, Qureshi F M, Ahmad I, Jawa A, Sheikh A, Raza A, Fazid S & Jadoon Z. 2019a. Diabetes Prevalence Survey of Pakistan (DPS-PAK): prevalence of type 2 diabetes mellitus and prediabetes using HbA1c: a population-based survey from Pakistan. BMJ open. 9(2): e025300.
15. Juster-Switlyk K & Smith A G. 2016. Updates in diabetic peripheral neuropathy. F1000Res. 5.
16. Gray N, Picone G, Sloan F & Yashkin A. 2015. Relation between BMI and diabetes mellitus and its complications among US older adults. South Med J. 108(1): 29-36.
17. Iqbal Q, Ul Haq N, Bashir S & Bashaar M. 2017. Profile and predictors of health related quality of life among type II diabetes mellitus patients in Quetta city, Pakistan. Health Qual Life Outcomes. 15(1): 142.
18. Islam S M, Alam D S, Wahiduzzaman M, Niessen L W, Froeschl G, Ferrari U, Seissler J, Rouf H M & Lechner A. 2015. Clinical characteristics and complications of patients with type 2 diabetes attending an urban hospital in Bangladesh. Diabetes Metab Syndr. 9(1): 7-13.
19. Pan H Y, Guo L & Li Q. 2010. Changes of serum omentin-1 levels in normal subjects and in patients with impaired glucose regulation and with newly diagnosed and untreated type 2 diabetes. Diabetes Res Clin Pract. 88(1): 29-33.
20. Wan W, Li Q, Zhang F, Zheng G, Lv Y, Wan G & Jin X. 2015. Serum and vitreous concentrations of omentin-1 in diabetic retinopathy. Disease markers. 2015
21. Yasir M, Senthilkumar G P, Jayashree K, Ramesh Babu K, Vadivelan M & Palanivel C. 2019. Association of serum omentin-1, apelin and chemerin concentrations with the presence and severity of diabetic retinopathy in type 2 diabetes mellitus patients. Archives of physiology and biochemistry. 1-8.
22. Senthilkumar G P, Anithalekshmi M S, Yasir M, Parameswaran S, Muthu Packirisamy R & Bobby Z. 2018. Role of omentin 1 and IL-6 in type 2 diabetes mellitus patients with diabetic nephropathy. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 12(1): 23-26.
23. Qasem A, Farage S, Elmesallamy F A & Elsaid H H. 2015. Association of plasma omentin-1 level with insulin resistance in chronic kidney disease patients. Egyptian Journal of Obesity, Diabetes and Endocrinology. 1(2): 72.
24. Korany M A, Sonbol A & Elgouhary S M. 2018. Omentin-1 and diabetic retinopathy in type 2 diabetic patients. Alexandria journal of medicine. 54(4): 323-326.
25. Tuttolomondo A, Di Raimondo D, Casuccio A, Guercio G, Del Cuore A, Puleo M G, Della Corte V, Bellia C, Caronia A & Maida C. 2019. Endothelial Function, Adipokine Serum Levels, and White Matter Hyperintesities in Subjects With Diabetic Foot Syndrome. The Journal of Clinical Endocrinology & Metabolism. 104(9): 3920-3930.

This article may be cited as: Hanif M.S, Nadeem A., Naureen T, Correlation of serum Omentin-1 levels with Diabetic peripheral neuropathy in Type-2 diabetes mellitus patients: A Cross-Sectional Study. Pak J Med Health Sci, 2023; 17(7): 207-210.