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Evaluating the Role of Visfatin and Metabolic Markers in Osteoarthritis Cases with Diabetes Mellitus in Sulaimani City, Kurdistan Region, Iraq

Hersh Ibrahim Rashid[1], Attallah Omar Qasem[1], Kadamkheer Tawfiq Aziz[1], Sara Omar Hassan[2]

[1]Public Health Department, Sulaimani Technical Medical Institute, Sulaimani Polytechnic University, Sulaymaniyah, Iraq.
[2]Radiology Department, Sulaimani Technical Medical Institute, Sulaimani Polytechnic University, Sulaymaniyah, Iraq.

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ABSTRACT

It was demonstrated that neuropathy was due to impaired glucose control levels in the blood, which caused pain due to osteoarthritis. Early, undetectable levels of biological alteration are characteristic of both osteoarthritis and diabetes mellitus, which are chronic diseases. This study was conducted to investigate serum visfatin levels and their association with parameters in patients with osteoarthritis. Sixty-eight patients with diabetes mellitus and osteoarthritis are included in the present research to examine the effect of visfatin and associated clinical markers in these cases. Twenty healthy control volunteers were used to compare the outcomes. Accurate kits were used to determine visfatin and related parameters. The present study's findings revealed increases in visfatin, glucose, HbA1c, and insulin resistance levels among patients, while insulin levels decreased. It appears that visfatin has been established to have a physiological effect on osteoarthritis in patients suffering from type II diabetes mellitus.

Corresponding Author:

Hersh Ibrahim Rashid

Public Health Department, Sulaimani Technical Medical Institute,
Sulaimani Polytechnic University, Sulaimaniyah City, Sulaimaniyah Governorate, Iraq.
Email: hersh.ibrahim@spu.edu.iq

1. INTRODUCTION

Osteoarthritis (OA) is a chronic biomechanical illness characterized by pain and progressive degeneration of bone, cartilage, muscles, and ligaments, and is strongly associated with inflammatory and catabolic changes [1, 2]. The most common disease in developing countries is osteoarthritis, according to the World Health Organization [3]. OA progression and development have been related to risk factors like metabolic disorders, sex, joint mechanical stress, some genetic profiles, and aging, similar to inflammation [1, 2]]. Visfatin was linked with numerous OA metabolic changes, specifically insulin resistance[4, 5], and type 2 diabetes mellitus (T2DM) [6, 7, 8]. Adipokine, a visfatin engaged in catabolism and inflammation [9, 10], has been powerfully related to numerous pathological features and risk factors of diabetes mellitus and osteoarthritis (OA) [8, 11]. The amount of visfatin was established to be higher in individuals with insulin resistance (HOMA-IR)[12]. One study investigating the relationship between DM and OA explored a range of related factors, including insulin, leptin, visfatin, and HbA1c [13]. Importantly, visfatin has also been linked as a risk factor for OA and type 2 diabetes.

Even after controlling for body mass index, visfatin plasma levels are noticeably greater in patients with type 2 diabetes mellitus than in healthy individuals [8]. Some research has linked the worsening of T2DM glucose intolerance to even greater plasma levels of visfatin[10]. Overall, visfatin has been revealed to be a serious component included in all main OA risk factors and comorbidities[5] . A widespread meta-analysis additionally confirmed the association of metabolic syndrome with visfatin, T2DM, insulin resistance, and obesity[5].

1.1 Visfatin Interaction with Osteoarthritis (OA) Risk Factors.

The pre-B colony boosting factor (PBEF) is the name given to the adipokine visfatin.[14], it is found in multiple tissues [15], including those from the musculoskeletal system (cartilage, muscle, synovium, and bone)[14, 16]. Nonetheless, the adipose tissue, including subcutaneous fat and visceral fat, is the most serious visfatin source[15]. Importantly, visceral adipose tissue releases more visfatin than subcutaneous fat.[15]. Visfatin is a class II phosphoribosyl transferase homodimer of approximately 120 kDa[17, 18]. The functions of the 2.0 kb and 4.0 kb transcripts are unknown; however, the two 52 kDa 473-residue polypeptides were discovered from the 2.4 kb mRNA. Two distinct promoters measure the transcription of the human visfatin gene (7q22; 34.7 kb), and alternative splicing modifies it.[19] (Figure 1). At the cellular level, visfatin is excreted into the extracellular space by an indistinct mechanism [20, 21]. While subcellular distribution is still under debate[22], visfatin has been known in the nuclei [23] connected with cell cycle regulation[22], and in the cytosol[24] related with its enzymatic activity as nicotinamide phosphoribosyl transferase (NAMPT)[16]. Visfatin and (NAMPT) catalyze the conversion of nicotinamide (NAM) to nicotinamide mononucleotide (NMN) by SN1 reaction. Subsequently, NMNAT, as a catalyst in nucleotide transfer reaction, converts AMP from ATP added to NMN to NAD^+ formed (Figure 2). This process has to do with the production of NAD+27. Therefore, visfatin is bound to affect any NAD+ dependent function, including cell adhesion[25], redox potential[26], and oxidative stress[27, 28], but likewise aging[29, 30], DNA repair[31],; it also regulates aging.

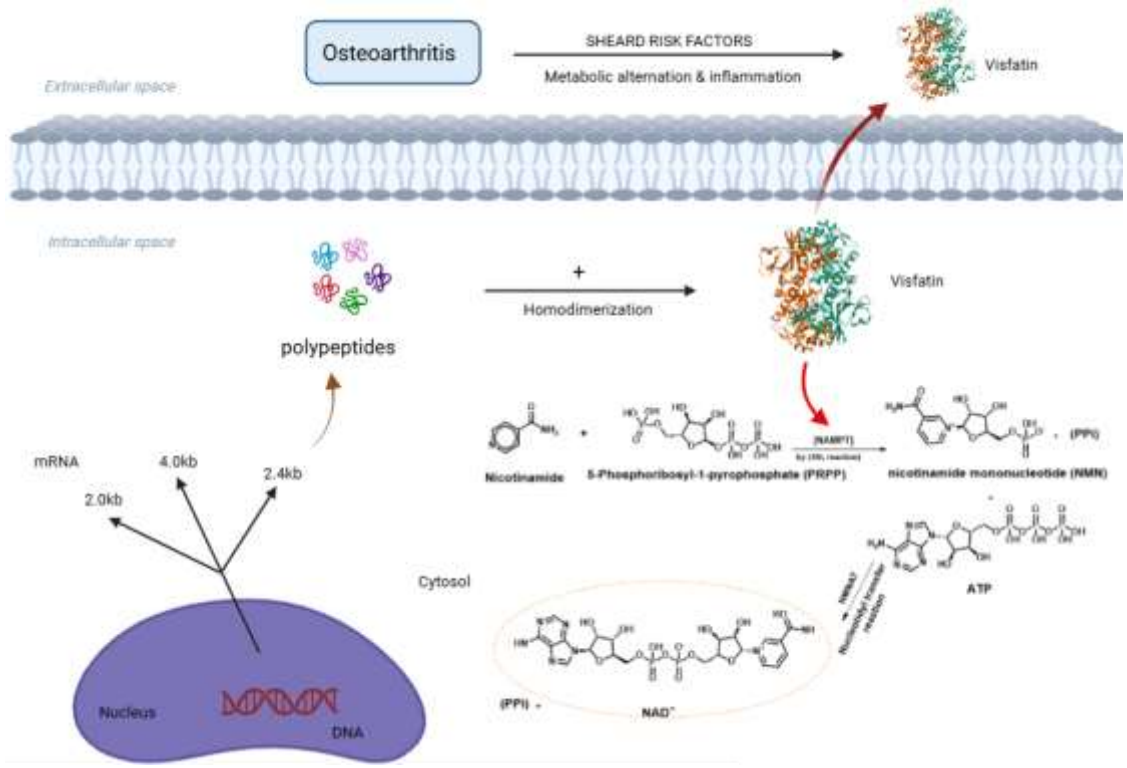

Figure 1. "Visfatin Interaction with Osteoarthritis (OA) Risk Factors: Mechanisms of Intracellular Synthesis and Enzymatic Activity"

1.2 The Development of Osteoarthritis and Type 2 Diabetes Mellitus

Type 2 diabetes mellitus (T2DM) is a chronic metabolic condition that has been associated with many problems[32]. There is now growing epidemiological experimental evidence suggesting that T2DM is an independent risk factor for the advancement of OA[33]. Less is known, however, about the molecular processes that underlie the link between OA and type 2 diabetes[8]. Since local inflammation is crucial to both T2DM and OA illnesses, it is hypothesized that there might be a significant mechanistic relationship [34]. For instance, the synovitis in OA may be worsened by the augmented level of inflammatory prostaglandins, adipokines, and cytokines, which can likewise be observed in T2DM tissues[35]. Moreover, hyperglycemia is the major trigger of joint degradation in OA, and it also has a tight connection with inflammation[36]. Local hyperglycemia raises the amount of progressive glycation end products (AGEs), which in turn trigger the synthesis of pro-inflammatory and catabolic mediators[37]. This can cause the cartilage matrix to become disorganized, resulting in tissue remodeling, matrix stiffness, and subchondral bone loss. [38]. Moreover, low-grade systemic inflammation brought on by hyperglycemia may accelerate the course of OA. [39, 40]. Thus, the hyperglycemia-induced inflammation may underlie the OA phenotypes linked with T2DM[41].T2DM prompts a pathological role on OA effected through two significant pathways:

(1) chronic hyperglycemia, which increases the production of AGEs, oxidative stress, and pro-inflammatory cytokines in joint tissues while also inhibiting the latent chondrogenic differentiation of different stem cells, thereby weakening the already compromised cartilage restoration in OA; and (2) insulin resistance, which has an impact both locally and systemically through low-grade inflammation [6].

2. MATERIALS AND METHODS

All samples were collected from Sulaimani city/Kurdistan region, Iraq, from March 2025 to May 2025. Experiments were conducted at the Diabetes and Endocrine Center.

Chemicals: Human Visfatin Kit from CUSABIO, Human Insulin Kit (DRG), HbA1c (BioRAD), Human Insulin-like Growth-1 (IMMUNOTECH), Gls Kit (RANDOX),

Assay techniques used: Two bioassays were applied to the determination of parameters studied; they were ELISA and RIA. In addition, enzymatic and colorimetric determinations were also applied.

Sampling: These included 68 patients who were suffering from osteoarthritis (OA) and type II diabetes mellitus (T2DM). Their age ranged between 40-60 years, and they were divided into three groups: 24 cases with OA only, 20 cases with DM only, and 24 cases with both OA and DM. Controls were (20), their age ranged between (30-50 years), and they consisted of females and males; they were also healthy, and they had no history of disease.

Blood Samples Collection: For each case, take 10 mL of blood by using a disposable syringe after 12-15 hours of fasting. After that, the blood was divided according to testing, as shown in Figure 2. Anticoagulant compound (EDTA) (1.5 mg/mL) into the first aliquot test tube. This blood was processed in less than three hours and was used to determine HbA1c. Plasma blood glucose was determined from the second aliquot. After being distributed in a simple tube, the third aliquot was allowed to coagulate at room temperature (22°C) for about an hour; Then, the serum was collected after centrifuging the sample at 3000 rpm for 10 min.
The samples stored in the freezer (-20ºC) were divided into three aliquots (500µl).

Measurement of Insulin Resistance: The methodology was taken from a different research, such as using the publicly available HOMA2-Calculator software, the Evaluation of the Homeostasis Model HOMA insulin sensitivity (HOMA2-S%), HOMA beta cell function (HOMA2-B%), and two insulin resistance parameters (HOMA2-IR) were calculated [42].
Determination of Serum Visfatin: By the use of a CUSABIO kit, serum visfatin was measured quantitatively in vitro using an enzyme-linked immunosorbent assay. (Catalog- E08940h). Horseradish Peroxidase (HRP) coupled with visfatin and avidin is incubated in the test before each well receives a TMB (3,3',5,5' tetramethyl-benzidine) substrate solution.
Calculations: A standard curve generated in the same assay as the sample was used to interpolate all the findings.
Determination of Serum Insulin Level: A protocol of (Frier et al, 1981)[43] was applied for Insulin level determination using the DRG Insulin ELISA kit.

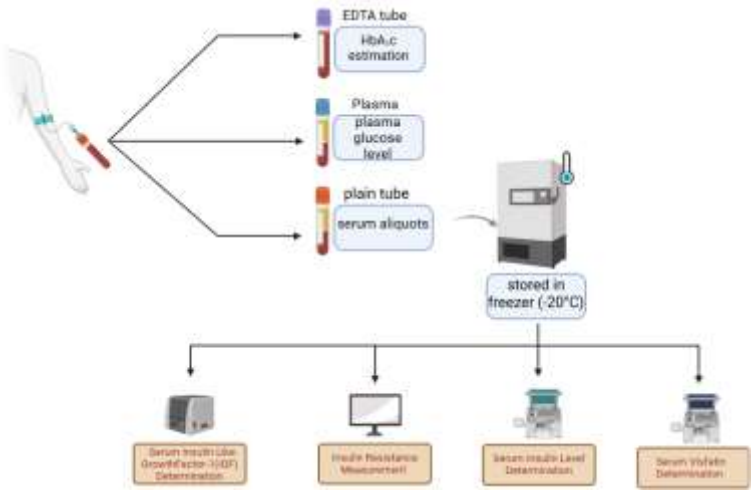

Figure 2. Sample Processing and Analytical Procedures for Assessing Visfatin, Insulin, Glucose, and HbA1c Levels"

2.1 Serum Insulin-Like Growth Factor-1 (IGF) Determination

Principle of Assay: A Radioimmunoassay (RIA) technique was used to determine Insulin-Like Growth Factor-1, using I125 as a radioactive tracer to count bound antigen, which is proportional to the IGF-1 sample concentration. This technique was applied by IMMUNOTECH SAS-130 Ave).

Determination of Plasma Glucose: Glucose oxidase (GOD) oxidizes glucose to gluconate and hydrogen peroxide. This is a principle of the enzymatic colorimetric test, as described by Barham and Trinder (1972)[44]. The level of plasma glucose was found by using this equation:

$$Fasting\ plasma\ Glucose\left({}^{mg}/_{dl}\right) = \left(\frac{Optical\ Density\ Of\ Sample}{Optical\ Density\ Of\ Standard}\right) * Concentration\ of\ standard$$

Determination of Glycated Hemoglobin: The HPLC analytical methodology is necessary for the concept to work. HPLC principles are used in the Bio-Rad VARIANT Hemoglobin A1c program. Lipemia, temperature changes, and labile A1C do not interfere with the quick and accurate separation of HbA1c.
Analysis Data: The SPSS-17 system was used for statistical analysis. All data was represented in a simple statistical analysis of numbers, mean, range, and standard deviation. The Student-t-test for the difference between two independent means was used for these statistical procedures referenced paper. Authors refer to a table number in the results section, for example, Table 2 indicates that healthcare professionals demonstrate good practice.

3. RESULTS AND DISCUSSION

The following data explain the amount of serum visfatin and are related to clinical parameters during the present study. Their results were estimated by Mean ± SD. The outcomes reflect a significant rise in visfatin (P-value <0.05) in each sick group's comparison to the control group. Correspondingly, the consequences reflect a significant elevation in glucose, HOMA-IR, and HbA1c concentrations (P-value <0.05) compared with the control. The patient groups were suffering from T2DM, as confirmed in Tables 3 and 4. Insulin hormone levels have diminished in cases have Osteoarthritis or diabetes mellitus or both of them compared to the control group, with these decreases nearly halving. The reductions were not revealed to be significant when comparing insulin levels with the control, as shown in Figure 3.

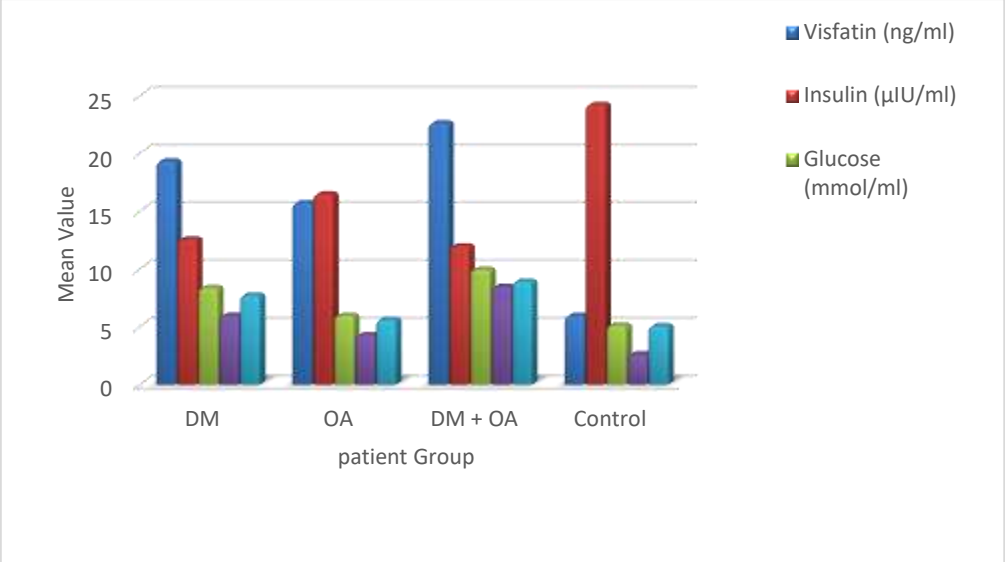

Figure 3. Comparison of Clinical Parameters Across Patient Groups

As an adipokine, visfatin has been demonstrated to play many roles in the human body. It was of importance in the mediating network among metabolic disorders and inflammatory autoimmune diseases. Visfatin and NAMPT facilitate the formation of NMN by the SN1 reaction mechanism from nicotinamide, completed by NMNAT-catalyzed NAD^+ synthesis. It has been shown that visfatin has an effect on an increased level of RA, MMPs, and PGE2, and increases levels of pro-inflammatory cytokine [13]. Research reported by Busso et al., 2008[45], clarified that prevention of visfatin in inflammatory illness decreases the severity of collagen-induced arthritis. Additionally, the majority of research on metabolic illnesses has shown elevated levels of visfatin in the bloodstream in various clinical circumstances, like metabolic syndrome, T2DM, and obesity [46], accordingly, an anticipated decreased level of insulin was detected in all patient groups (Table 2).

Correspondingly, research has confirmed the significant role of visfatin in other disorders and its behavior as a regulatory factor [47, 48]. The conclusions of the present study were found to agree with the literature mentioned above. It was also verified that there is disagreement among research reports about the level of visfatin/PBEF/Nampt in these cases of disease, where circulating levels have also been found.

Table 1. The amount of visfatin in each patient group compared with the control group

Variables	Visfatin levels (ng / ml)			
	diabetes mellitus	Osteoarthritis	diabetes mellitus+ Osteoarthritis	Control
NO. of case	20	24	24	20
Mean ± SD	19.35 ± 5.93	15.73 ± 6.87	22.65 ± 8.06	5.97± 3.09
Range	7.01 – 32.21	8.76 – 31.68	8.25 – 35.73	0.68 – 13.85
P against control	0.0001	0.0001	0.0001	
P against total	0.0001			

Table 2. The amount of insulin in each patient group compared with the control group

Variables	Insulin levels (µIU / ml)			
	diabetes mellitus	Osteoarthritis	Diabetes mellitus+ Osteoarthritis	Control
NO. of case	20	24	24	20
Mean ± SD	12.59 ± 5.26	16.50 ± 9.45	11.99 ± 6.58	24.24 ± 2.49
Range	3.6 – 32.0	4.8 – 50.1	7.1 – 117.8	2.3 – 22.4
P against control	0.989	0.322	0.137	
P against total	0.20			

Table 3. The amount of blood glucose in each patient group compared with the control group

Variables	Glucose concentration (mmol/ml)			
	diabetes mellitus	Osteoarthritis	Diabetes mellitus+ Osteoarthritis	Control
NO. of case	20	24	24	20
Mean ± SD	8.38 ± 3.28	5. 97 ± 1.15	9.97 ± 5.29	5.13 ± 0.59
Range	4.10 – 25.60	4.40 – 9.40	4.40 – 17.40	4.00 – 6.00
P against control	0.003	0.019	0.0001	
P against total	0.0001			

Table 4. The amount of HOMA–IR in each patient group and compared with the control group

Variables	Concentration of HOMA–IR			
	diabetes mellitus	Osteoarthritis	Diabetes mellitus+ Osteoarthritis	Control
NO. of case	20	24	24	20
Mean ± SD	6.00 ± 5.69	4.30 ± 2.63	8.49 ± 1.04	2.65 ± 1.27
Range	1.2 – 25.0	1.10 – 14.6	1.6 – 39.7	0.5 – 5.1
P against control	0.078	0.048	0.009	
P against total	0.003			

Table 5. The amount of HbA1c in each patient group compared with the control group

Variables	% HbA1c Concentration			
	diabetes mellitus	Osteoarthritis	Diabetes mellitus+ Osteoarthritis	Control
NO. of case	20	24	24	20
Mean ± SD	7.74 ± 2.13	5.63 ± 0.49	8.93 ± 2.00	5.08 ± 0.53
Range	5.00 – 12.00	4.20 – 6.30	6.50 – 13.20	4.40 – 6.00
P against control	0.0001	0.006	0.0001	
P against total	0.0001			

4. CONCLUSION

The research study exhibited that the amount of blood glucose, HbA1c, visfatin, and insulin resistance increases, and the level of insulin decreases. Similarly, visfatin has been established to have a physiological influence on osteoarthritis in patients suffering from diabetes.

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BIOGRAPHIES OF AUTHORS

M.Sc Hersh Ibrahim Rashid is Assistant lecture at Sulaimani Technical Medical Institute, Sulaimani polytechnic University, Iraq. He received the B.Sc. degree in chemistry science from the University of sulaimani and M.Sc. degree from University of Kurdistan, IRAN. He Holds in Chemistry Science with specialization in organic chemistry and biochemistry. His research areas are chemistry and drug design. He has published several scientific papers in national, international conferences and journals. He can be contacted at email: hersh.ibrahim@spu.edu.iq

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Attallah Omar Qasem is an assistant professor at Sulaimani Technical Medical Institute, Sulaimani polytechnic University, Iraq. Her research areas are public health. he has published several scientific papers in national, international conferences and journals. he can be contacted at email: atta.kasem@spu.edu.iq

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