Effect of S1P and GSN for osteoporosis patients

Noor Ali Nemaha[1], Hanan Jassim Hammod[2*]

Abstract

Osteoporosis is a metabolic bone disease that results, at the cellular level, in osteoporotic bone resorption that is irreplaceable by osteogenesis of osteoblasts. This leads to weak bones and causes osteoporosis, which leads to an increased risk of fractures. Aim of Study: the current study aimed to detected biomarkers in patients with osteoporosis and it association with some physiological status have been a study because increase incidence of osteoporosis, for both genders which might also help in early diagnosis of case of osteoporosis to prevent development of complication, this achieved by: Estimation of some biomarkersS1P and GSN .Result :The GSN parameter in the current study was highly significant increase in osteoporosis age group (41-50 y) patients (86.26±9.06) than in control age group (41-50 y) (24.07±1.64) according to p-value (0.0001). The SIP parameter in the current study was highly significant increase in osteoporosis age group (41-50 y) patients (2398.36±218.65) than in control age group (41-50 y) (1046.66±40.71) according to p-value (0.0001). The GSN parameter in the current study was in two group pre-menopause and post –menopause is highly significant increase in osteoporosis pre-menopause group patients (83.29±6.44) and post-menopause in patients (80.50±14.32) according to p-value (0.067) than pre–menopause in control (23.76±1.78) and post –menopause in control (29.12±4.87) according to p-value (0.123).The S1P parameter in the current study was in two group pre-menopause and post –menopause is highly significant increase in osteoporosis pre-menopause group patients (2508.96±166.48) and post-menopause in patients (2415.70±469.02) according to p-value (0.346) than pre–menopause in control (1067.46±34.42) and post –menopause in control (1026.76±43.22) according to p-value (0.785).As shown in figure(6), the statistics results of these two parameters showed correlation between the mean level of Age and the mean level of protein S1P (P-value = 0.018).

KeyWords: Effect, Patients, GSN

DOI Number: 10.14704/nq.2022.20.8.NQ44315 **NeuroQuantology2022; 20(8):2842-2850**

Introduction

Osteoporosis is the most common chronic metabolic bone disease, and it is characterized by increasing osteoporosis. It affects people of all ages, genders, and gender identities, but it is more common among elderly individuals and women. With the aging of the population and the extension of life spans, several variables that impact bones, such as aging and menopause, are becoming more prevalent .According to the International Osteoporosis Foundation, one in every three women over 50 and one in every five men over 50 may suffer a bone fracture as a result of osteoporosis at some time in their lives. Osteoporosis is growing more prevalent throughout the world (9). Osteoporosis can be primary or secondary to other diseases that lead to bone loss. Type I osteoporosis in rare cases, the process of bone formation is normal in this type of osteoporosis, which leads to more bone loss (12). Sphingosine-1-phosphate (S1P) is a naturally occurring, biologically active sphingosine lipid that regulates biological and cellular processes such as migration, proliferation, differentiation, and survival, and has been linked to illnesses. According to research, S1P has been linked to a number of bone illnesses, including osteoporosis. However, the effects of S1P, particularly on bone metabolism, are still being investigated (4). The gelsolin (GSN) superfamily consists of actin remodeling proteins that include gelsolin, which is a multifunctional Ca2+ regulator protein. It interacts with filamentous actin and monomeric actin and has a barbed end cap (7).

Corresponding author: Hanan JassimHammod
Address: [1]Colleage of Health and Medical Techniquse /Kufa/Al-Furat Al-Awsat Technical University/Iraq,[2]Babylon Technical

Institute/Kufa
E-mail: dr.hanan.jh@gmail.com

Materials And Methods

1-Patients

The research was carried out at Al-Sadr Teaching Hospital's Physiotherapy Center-Osteoporosis Department from December 1 to January 9.The study included 90 participants, including 45 osteoporosis patients and 45 healthy adults who served as controls. Patients were diagnosed by specialists based on their family histories, age, height, weight, and a few unambiguous clinical criteria, which were then confirmed by the DXA (dual-energy x-ray absorptiometry) instrument and other tests. As various vitamin D and calcium laboratory tests

2 -Control

The controls provided blood samples that were equivalent to those of the patients in terms of sex and age, but they did not have any hereditary illnesses, infections, or chronic conditions.

3- Exclusion criteria

When the samples were taken from patients and controls, some of them were left out since they could change the results. In this study, samples with (heart failure, vitamin deficiency, warfarin intake, chemotherapy, kidney failure, surgery, removal of the small intestine, drug treatment, cephalosporin antibiotics) were included because these conditions could affect the results of protein S1P and GSN in the samples.

Methods

1 -Sample Collection

Each control and osteoporosis patient had 5 mL of venous blood drawn in this investigation. Ethyl alcohol was used to sanitize the skin. The patient was being readied for a blood transfusion at this time. Blood was drawn and deposited in tubes as follows: The tube included a separating gel in which 3 ml was poured and left to clot for 10-15 minutes at room temperature before being centrifuged for 5 minutes at 5000 rpm to obtain the serum. The serum was collected for testing purposes (S1P and Gelsolin).

2 -BMI (Body Mass Index)

The BMI is a metric that uses a person's weight and height to assess how lean or obese they are. It is used to determine the weight of tissue.

3- ELISA (Enzyme Linking Immunosorbent Assay)

The amounts of the proteins S1P and GSN in the plasma of healthy controls and osteoporosis patients were measured using ELISA kits.

4. Human Protein Gelsolin Elisa Kit

The level of human protein gelsolin was evaluated using the enzyme-linked immunosorbent assay (ELISA) method, as described in the Elabscience, China Cat-No. E-EL-H1786 manufacture instructions

5. Human Protein Sphingosine-1-phosphate (S1P) ELISA Kit

Elabscience Biotechnology Co., Ltd. provided a specific kit for testing human ProteinSphingosine-1-phosphate quantities in serum. E-EL-H1786 is a catalog number

Results and Discussion

Results

This study was conducted on a total 90 person composed of two groups. The first group was the patient group, which consists of 45 patients with Osteoporosis, were collected from patients attended to " Physiotherapy Center - Osteoporosis Department in AL-Sadder medical city in Al-Najaf Governorate/ Ministry of Health/Iraq, in the period from 1st of December to the 9th of January. with an age ranging between (34-68) years old; and The second group is the control group (Non-osteoporosis), which consists of 45 with no osteoporosis, also from the same place with age ranging (30-68) years old. Patients were diagnosed by specialist physicians based on family histories, age, height, weight and some clear clinical parameters and confirmed bythe DXA (dual-energy x-ray absorptiometry) device.

Table 1: General characteristics of patients and healthy groups.

Group		Patient		Healthy		p-value
		N	%	N	%	
Gender	Male	10	22.2	13	28.9	0.03*
	Female	35	77.8	32	71.1	
Age	20-40	7	15.6	15	33.3	0.04*
	41-60	25	55.5	15	33.3	
	<60	13	28.8	15	33.3	
BMI (kg/M2)	Normal	12	26.7	11	22.4	0.023*
	over-weight	17	37.8	13	28.9	
	Obesity	36	35.6	21	46.7	
Smoking	No	28	62.2	24	53.3	0.039*
	Yes	17	37.7	21	46.6	
Menopause	Pre-menopause	14	31.2	21	65.6	0.001**
	Post-menopause	31	68.8	11	34.3	

*Significant different at($p<0.05$)
**Significant different at($p<0.01$)

Biochemical Results

Table2: Biochemical parameter in patient and control in study on osteoporosis.

Group Parameter	Patient	control	P-value
GSN ng/ml	63.74±4.59	25.50±1.45	0.0001**
S1P pg/ml	2445.13±137.17	1031.03±19.38	0.0001**
Ca mg/dL	6.92±0.20	8.75±0.12	0.001*
ALP Iu/L	150.47±17.44	60.07±3.08	0.001*

*Significant different at($p<0.05$)
**Significant different at($p<0.01$)

As shown in the table above, there is a significant difference between the patient and control groups in all parameters (P-value) less than 0.0001).

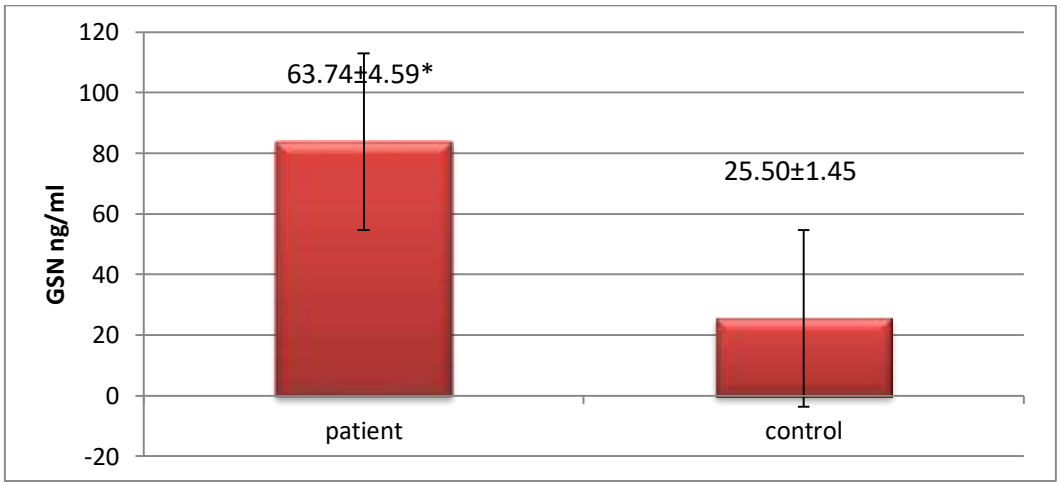


Figure 1: Comparisons of serum GSN between patient and control groups in osteoporosis

The GSN parameter in the current study was highly significantly increased in osteoporosis patients (83.74±4.59) than in control group (25.50±1.45) according to p-value (0.0001).

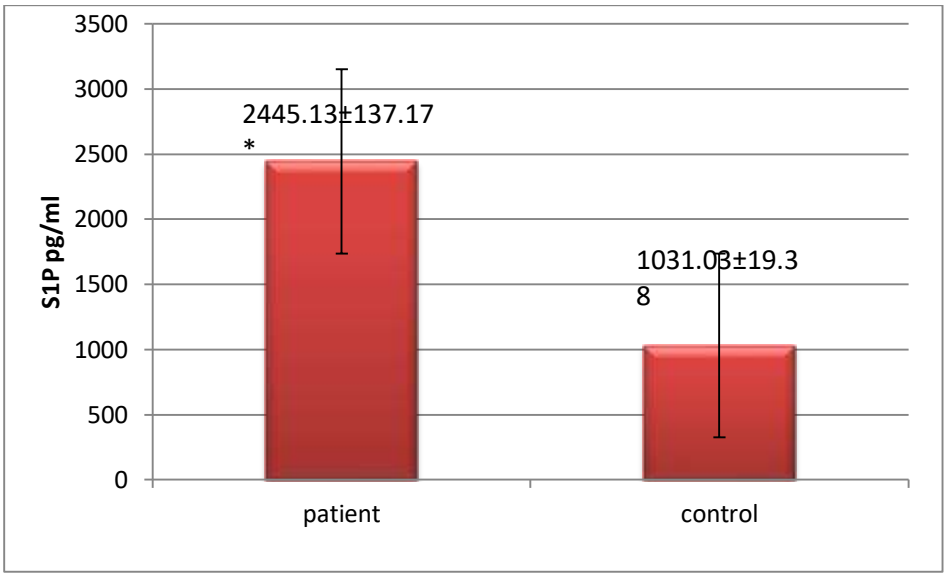


Figure 2: Comparisons of serum s1p between patient and control groups in osteoporosis

The S1P parameter in the current study was highly significant increase in osteoporosis patients (2445.13±137.17) than in control group (2445.13±137.17) according to p-value (0.0001). The current study agreed with a study that found a significant increase in patients

Table3: Biochemical parameter in patient and control in study on osteoporosis as age groups comparison.

Parameter	group	20-40 y	41-50 y	<60 y
GSN ng/ml	patient	77.92±5.57	86.26±9.06	93.85±8.79
	control	29.59±3.08	24.07±1.64	22.86±2.39
	P-value	0.0001	0.0001	0.0001
S1P pg/ml	patient	1853.23±478.08	2398.36±218.65	2694.40±156.35
	control	1035.66±31.81	1046.66±40.71	1010.76±28.68
	P-value	0.019	0.0001	0.0001
Ca ng/ml	patient	6.67±0.48	6.80±0.34	7.14±0.27
	control	8.62±0.24	8.62±0.22	9.0±0.16
	P-value	0.001	0.0001	0.0001
ALP v/l	patient	121.50±48.59	129.49±28.77	179.50±24.03
	control	61.0±5.71	59.86±4.71	59.33±5.87
	P-value	0.0001	0.0001	0.0001

*Significant different at($p<0.05$)
**Significant different at($p<0.01$)

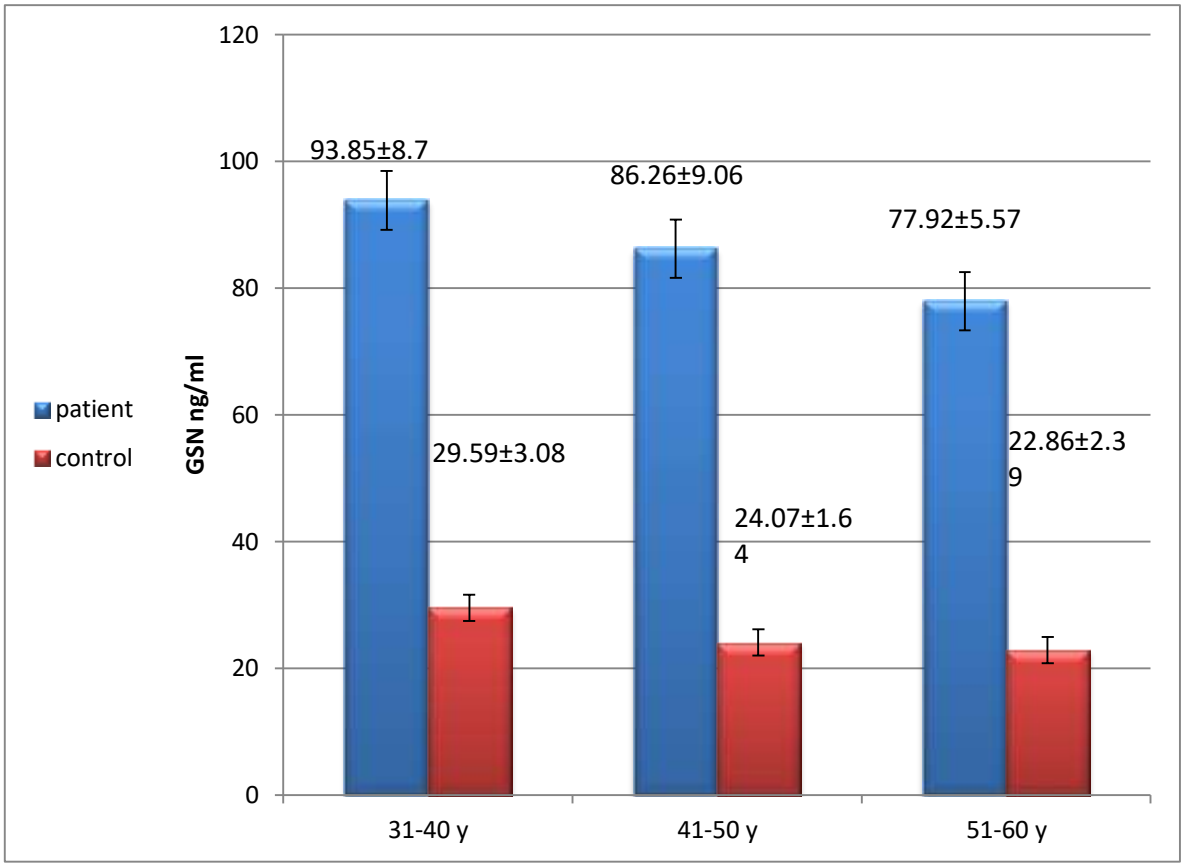


Figure 3: Comparisons of serum GSN between patient and control groups age in osteoporosis.

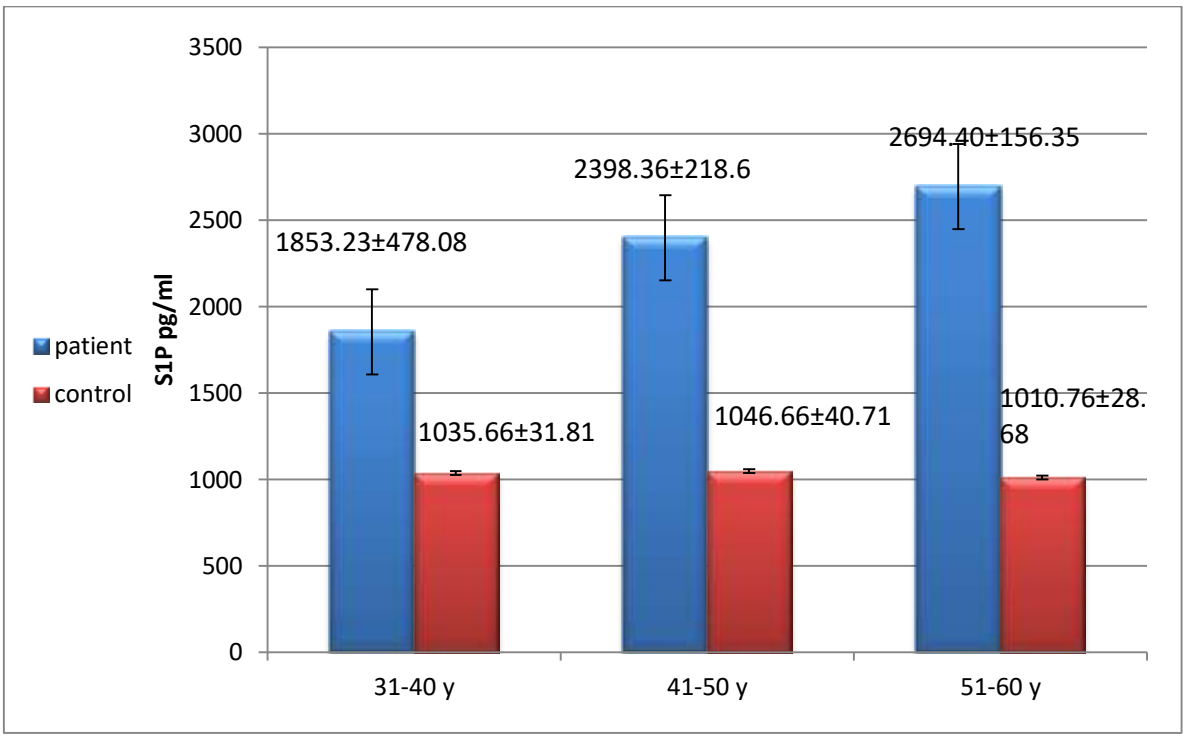


Figure 4: Comparisons of serum sphingosine-1-phosphate (S1P) between patient and control groups age in osteoporosis.

Table4. Biochemical parameter in patient and control in study on osteoporosis as pre-menopause and post-menopause groups comparison.

Parameter	Cycle	Patient	Control
GSN ng/ml	Pre	83.29±6.44	23.76±1.78
	Post	80.50±14.32	29.12±4.87
	P-value	0.067	0.123
S1P pg/ml	Pre	2508.96±166.48	1067.46±34.42
	Post	2415.70±469.02	1026.76±43.22
	P-value	0.346	0.785
Ca ng/ml	pre	7.18±0.28	8.74±0.17
	post	6.16±0.54	8.62±0.27
	P-value	0.533	0.675
ALP v/l	pre	344.49±25.78	60.35±4.62
	post	405.11±39.32	62.00±10.09
	P-value	0.234	0.768

*Significant different at($p<0.05$)
**Significant different at($p<0.01$).

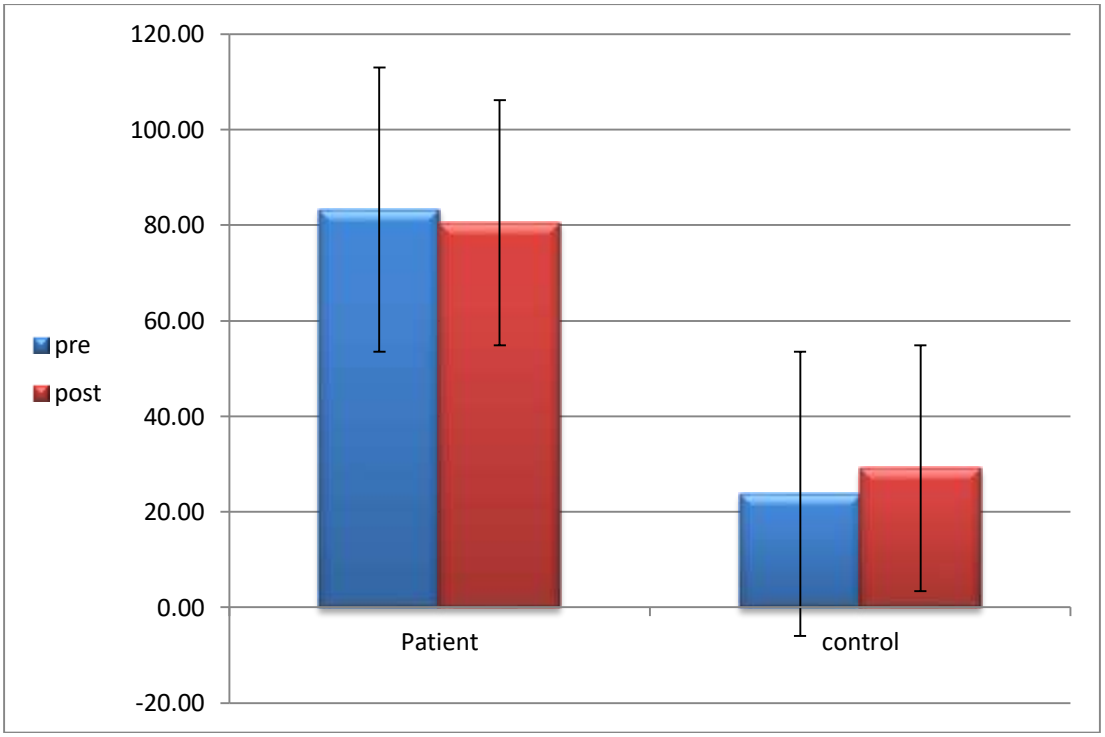


Figure 4-26: Comparisons of serum GSN between patient and control groups in pre-menopause and post-menopause in osteoporosis

.

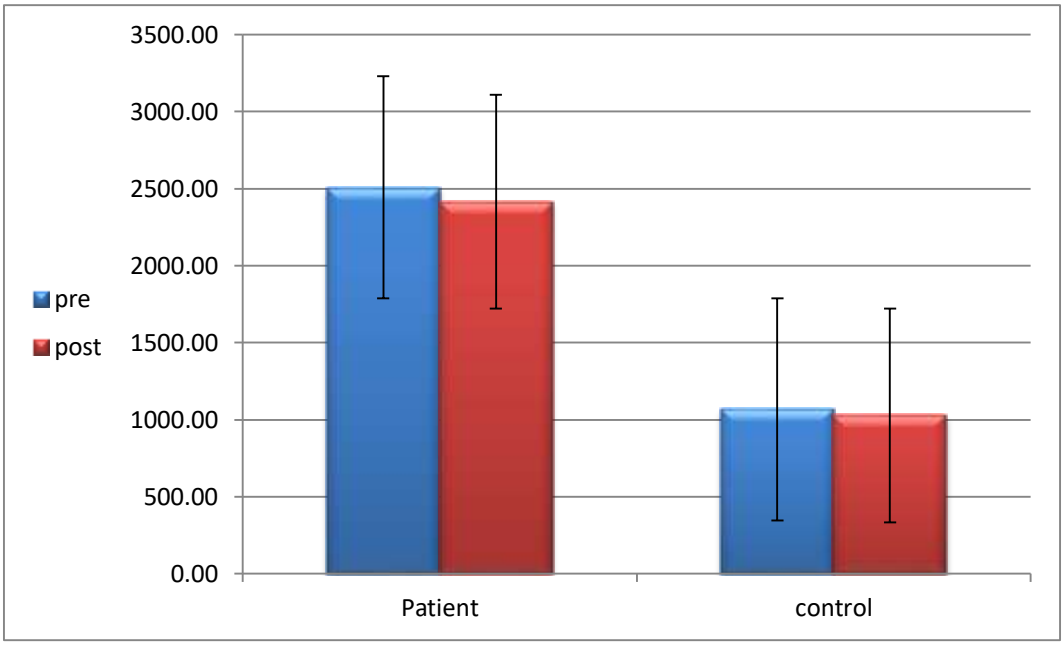


Figure 4-28: Comparisons of serum S1P between patient and control groups in pre-menopause and post-menopause in osteoporosis

Correlation between age and S1P

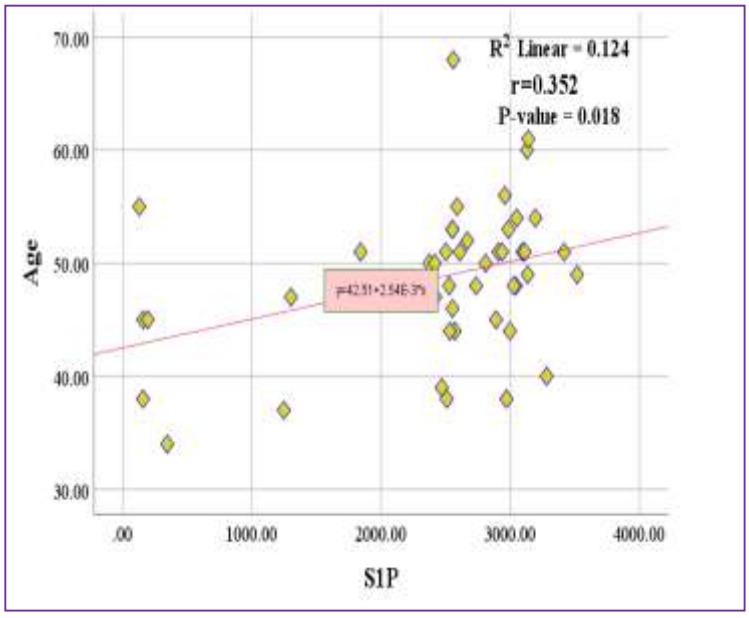


Figure 6: Correlation between Age and S1P protein.

As shown in figure(6), the statistics results of these two parameters showed correlation between the mean level of Age and the mean level of protein S1P (P-value = 0.018).

Discussion

Previous study showed that GSN deficiency would lead to the inability to produce podosomes, the abnormal actin cytoskeletal architecture; and the reduced rates of osteoclast motility; and blocked podosome-related signal transduction; and eventually cause decreased bone resorption; and increased bone mass and strength (11). Most studies published to date have consistently shown that high plasma S1P levels are associated with an increased prevalence and incidence of OFs (5) and that S1P levels positively correlate with the risk for OFs (8). It was found in my study of markers(S1P and GSN) that was conducted on patients and healthy people that it increases with age of patients

with osteoporosis, and it was found that the most increase occurs in the age group (41-50) years, which agreed with the researchers' study as explained„ .The GSN parameter in the current study was highly significant increase in osteoporosis age group (20-40 y) patients (77.92±5.57) than in control age group (20-40 y) (29.59±3.08) according to p-value (0.0001). The GSN parameter in the current study was highly significant increase in osteoporosis age group (41-50 y) patients (86.26±9.06) than in control age group (41-50 y) (24.07±1.64) according to p-value (0.0001). The GSN parameter in the current study was highly significant increase in osteoporosis age group (<60 y) patients (93.85±8.79) than in control age group (<60 y) (22.86±2.39) according to p-value (0.0001).

The SIP parameter in the current study was highly significant increase in osteoporosis age group (20-40 y) patients (1853.23±478.08) than in control age group (31-40 y) (1035.66±31.81) according to p-value (0.019). The SIP parameter in the current study was highly significant increase in osteoporosis age group (41-50 y) patients (2398.36±218.65) than in control age group (41-50 y) (1046.66±40.71) according to p-value (0.0001). The SIP parameter in the current study was highly significant increase in osteoporosis age group (<60 y) patients (2694.40±156.35) than in control age group (<60 y) (1010.76±28.68) according to p-value (0.0001).Plasma levels in women are affected by age. We observed an association between S1P levels and age, confirming previous studies.Biver, et al. has also showed raised levels of bone alkaline phosphatase in osteoporotic patients compared to normal, and these high levels may be associated with prevalent vertebral fractures (2). The GSN parameter in the current study was in two group pre-menopause and post –menopause is highly significant increase in osteoporosis pre-menopause group patients (83.29±6.44) and post-menopause in patients (80.50±14.32) according to p-value (0.067) than pre–menopause in control (23.76±1.78) and post –menopause in control (29.12±4.87) according to p-value (0.123).The discovered, validated that plasma GSN levels were significantly higher in extremely low BMD subjects than high BMD in postmenopausal women (Wang et al., 2016).The S1P parameter in the current study was in two group pre-menopause and post –menopause is highly significant increase in osteoporosis pre-menopause group patients (2508.96±166.48) and post-menopause in patients (2415.70±469.02) according to p-value (0.346) than pre–menopause in control (1067.46±34.42) and post –menopause in control (1026.76±43.22) according to p-value (0.785). Higher sphingosine 1-phosphate (S1P) plasma levels are associated with decreased bone mineral density (BMD), and increased risk of prevalent vertebral fracture. So, we hypothesized that postmenopausal women with increased baseline plasma S1P levels have a greater risk for future incident fracture (osteoporosis-related fractures [ORFs]), In this study, we report a significant association between increased plasma S1P and incident fracture risk in a population of postmenopausal women (1). As shown in figure(4-33), the statistics results of these two parameters showed correlation between the mean level of Age and the mean level of protein S1P (P-value = 0.018). Thus, plasma S1P metabolism, clearance, and/or production were stable among the women studied. However, we did observe minor changes in the longitudinal plasma S1P levels. Such changes may be related to aging and not analytical variability because plasma S1P measurements were performed under standardized conditions using a validated assay. Plasma levels in women are influenced by age. We observed a positive association between S1P levels and age, confirming previous studies in Korean women(6).

Reference

Ardawi, M. M. et al. High plasma sphingosine 1-phosphate levels predict osteoporotic fractures in postmenopausal women: The Center of Excellence for Osteoporosis Research Study. J. Bone Metab. 25, 87–98 (2018).

Biver E, Chopin F, Coiffier G, Brentano TF, Bouvard B, Garnero P, et al. Bone turnover markers for osteoporotic status assessment?A systematic review of their diagnosis value at baseline in osteoporosis. Joint Bone Spine. 2012;79(1):20–25.

Föger-Samwald, U., Dovjak, P., Azizi-Semrad, U., Kerschan-Schindl, K., & Pietschmann, P. (2020). Osteoporosis: pathophysiology and therapeutic options. EXCLI journal, 19, 1017

Grewe, J. M., Knapstein, P. R., Donat, A., Jiang, S., Smit, D. J., Xie, W., & Keller, J. (2022). The role of sphingosine-1-phosphate in bone remodeling and osteoporosis. Bone Research, 10(1), 1-9

Kim, B.-J. et al. Plasma sphingosine 1-phosphate levels and the risk of vertebral fracture in postmenopausal women. J. Clin. Endocrinol. Metab. 97, 3807–3814 (2012).

Lee SH, Lee SY, Lee YS, et al. Higher circulating sphingosine 1-phosphate levels are associated with lower bone mineral density and higher bone resorption marker in humans. J Clin Endocrinol Metab. 2012;97:E1421–E1428.

Nag S., Larsson M., Robinson R. C., Burtnick L. D. (2013). Gelsolin: the tail of a molecular gymnast. Cytoskeleton 70 360–384. 10.1002/cm.21117

Song, H. E. et al(2020). Association of circulating levels of total

and protein-bound sphingosine 1-phosphate with osteoporotic fracture. J. Investig. Med. 68, 1295–1299 (

Sözen, T., Özışık, L., &Başaran, N. Ç. (2017). An overview and management of osteoporosis. European journal of rheumatology, 4(1), 46.

Wang, W. Y., Ge, B., Shi, J., Zhou, X., Wu, L. F., Tang, C. H., ... & Lei, S. F. (2018). Plasma gelsolin is associated with hip BMD in Chinese postmenopausal women. Plos one, 13(5), e0197732.5

Chellaiah M, Kizer N, Silva M, Alvarez U, Kwiatkowski D, Hruska KA. Gelsolin deficiency blocks podosome assembly and produces increased bone mass and strength. J Cell Biol. 2000; 148: 665–678. pmid:10684249].

Cifu, D. X. (2020). Braddom's physical medicine and rehabilitation E-book. Elsevier Health Sciences