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Polymorphisms of collagen 1A1 (COL1A1) gene and their relation to bone mineral density in postmenopausal women

Polimorfizm genu kolagenu 1A1 (COL1A1) i jego związek z gęstością mineralną kości u kobiet po menopauzie

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Abstract

Objectives: *The goal of this study was to evaluate the frequency of Sp1 +1245G>T (rs 1800012) and -1997G>T (rs 1107946) COL1A1 gene polymorphisms in postmenopausal women with osteoporosis and osteopenia as well as assessing their relations with the clinical parameters and parameters of bone turnover.*

Study design: *The study included 538 (236 postmenopausal and 302 healthy reproductive) Polish women. The postmenopausal group included women with osteoporosis (n=90), osteopenia (n=90), as well as healthy individuals (n=56). All women of reproductive age were healthy. BMD was marked in the L2-L4 lumbar region of the spine using dual energy X-ray absorptiometry (DXA). Genomic DNA was isolated from peripheral blood, the genotype frequency of investigated polymorphisms was determined by PCR-RFLP technique.*

Results: *The frequency of Sp1 +1245G>T and -1997G>T polymorphisms of COL1A1 gene showed no statistically significant differences between group with osteoporosis, osteopenia and correct T-score and women of reproductive age. In postmenopausal women it was found that osteopenia and osteoporosis were correlated with age, birth weight, age of last menses occurrence, height, body weight and BMI value. Clinical parameters in all groups of women did not show any statistically significant correlation with frequency of Sp1 +1245G>T and -1997G>T COL1A1 polymorphisms.*

Conclusions: *An evaluation of Sp1 +1245G>T (rs1800012) and -1997G>T (rs 1107946) COL1A1 polymorphisms showed any influence of these genetic variants on osteoporosis development in Polish postmenopausal women. The presented correlation between osteoporosis and age, birth weight, age of last menses occurrence, height, body weight and BMI value confirms the important role of environmental factors in disease etiology.*

Key words: **polymorphism** / **collagen 1A1** / **bone mineral density** /

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Streszczenie

Cel pracy: *Celem pracy była ocena częstości występowania genotypów polimorfizmów Sp1 +1245G>T (rs 1800012) i -1997G>T (rs 1107946) genu COL1A1 u kobiet po menopauzie z osteoporozą i osteopenią oraz ocena związku pomiędzy analizowanymi polimorfizmami a parametrami klinicznymi i parametrami obrotu kostnego.*

Materiały i metody: *Do badania włączono 538 (236 po menopauzie i 302 zdrowych kobiet w wieku rozrodczym) kobiet z populacji polskiej. Grupa kobiet po menopauzie podzielona została na kobiety z osteoporozą (n=90), osteopenią (n=90) oraz kobiety o prawidłowych wartościach T-score (n=56). BMD oznaczano w odcinku lędźwiowym kręgosłupa (L2-L4) za pomocą absorpcjometrii podwójnej energii promieniowania rentgenowskiego (DXA). Genomowy DNA izolowano z krwi obwodowej, częstość genotypów badanych polimorfizmów oznaczano z zastosowaniem techniki PCR-RFLP.*

Wyniki: *Częstość występowania genotypów polimorfizmów SP1 +1245G>T i -1997G>T genu COL1A1 w grupie kobiet po menopauzie z osteoporozą, osteopenią i prawidłowym T-score oraz kobiet wieku rozrodczym nie wykazała istotnych statystycznie różnic i była zgodna z prawem Hardy-Weinberga. U kobiet po menopauzie stwierdzono, że występowanie osteopenii i osteoporozy było skorelowane z wiekiem, masą urodzeniową, masą ciała kobiet, wiekiem wystąpienia ostatniej miesiączki i wartością BMI. Parametry kliniczne we wszystkich grupach kobiet nie wykazały istotnego związku z występowaniem obydwu polimorfizmów SP1 +1245G>T i -1997G>T genu COL1A1.*

Wnioski: *Analiza polimorfizmów Sp1 +1245G>T (rs1800012) oraz -1997G>T (rs 1107946) COL1A1 nie pokazała żadnego wpływu tych wariantów genetycznych na rozwój osteoporozy w grupie polskich kobiet po menopauzie. Prezentowana korelacja pomiędzy rozwojem osteoporozy a wiekiem, masą urodzeniową, wiekiem wystąpienia ostatniej miesiączki, wysokością, masą ciała i wskaźnikiem BMI potwierdza ważną rolę czynników środowiskowych w etiologii osteoporozy także w grupie polskich kobiet.*

Słowa kluczowe: **polimorfizmy** / **kobiety** / **menopauza** / **osteoporoza** / **osteopenia** /

Introduction

Studies focus on association between molecular basis of osteoporosis and disease progression constitute invaluable contribution to development of diagnostic solutions in prevention and treatment of osteoporotic changes. Polymorphism of selected genes, among them vitamin D3 receptor gene [1], osteoprotegerin (OPG) [2], toll-like receptors (TLR) [3], omentin [4], Wnt/β-catenin pathway/LRP5 protein [5] and also collagen [6] gene have been proved to be the strong factors of osteopenia and osteoporosis development. Individual osteoporosis candidate genes that require particular attention are collagen genes: COL1A1 and COL1A2.

COL1A1 gene encodes the pro-alpha1 chains of type I collagen, a major component of bone extracellular matrix. Mutations of this gene contribute to the development of many diseases including osteogenesis imperfect. The gene itself is believed to be osteoporosis candidate gene. Polymorphisms of the collagen type I, alpha 1 gene (COL1A1) have been studied extensively in relation to the loss of bone tissue. On this basis it is suggested that the COL1A1 Sp1 (+1245G>T; rs1800012) polymorphism is associated with osteoporotic fractures and bone mineral density (BMD). Most studies focus on this polymorphism in the first intron which is the binding site of transcriptional factor Sp1. The most promising research is on the importance and association between BMD and polymorphisms located in promoter of COLIA1 which include -1997G>T (rs1107946) and -1663indelT (rs2412298) and their correlation with Sp1 polymorphism [6, 7].

The aim of this study was to assess the frequency of polymorphisms: Sp1 (+1245G>T; rs1800012) and -1997G>T (rs 1107946) of COL1A1 gene in postmenopausal women with osteoporosis, osteopenia and normal T-score value in Caucasian women. Additional analysis was performed between both polymorphic COL1A1 variants and clinical parameters as well as bone turnover parameters.

Material and methods

Study groups

The subjects of the analysis were unrelated Caucasian Polish postmenopausal women (n=236, 58.5±5.9 years, 90 with osteoporosis, 90 with osteopenia, 56 with correct T-score), underwent their densitometry examination in Densitometry Centre at Poznan University of Medical Sciences between 2003-2007. Additionally, a group of Caucasian Polish women in childbearing age (n=302, 31.0±4.4 years) with correct T-score and no osteoporotic changes were enrolled to genetic testing. Patients provided their written consent and the study was approved by Bioethics Committee of Medical University of Poznan (1415/03, 158/06). Demographic and clinical data of the studied population are presented in Table I.

Bone mineral density was marked in the lumbar region of the spine from L1 to L4, using dual energy X-ray absorptiometry (DXA). Densitometric examinations were performed with LUNAR DPX 100 instrument (Lunar Copr., Madison, USA). The results of BMD examinations were given in g/cm² units and presented in the form of T-score and Z-score values. Normal result for bone mineral density in DEXA method was between 1 standard deviation from average age in relation to peak bone mass (T-score from +1 to -1). Mean bone mineral density was examined and compared to that of normal young adult, as well as to the age matched mean. Height and body weight were measured to arrive at body mass index (BMI), expressed in the established formula

(body mass/height^2). Moreover, each individual patient was interviewed in detail to obtain information regarding prescription drugs, diseases, age when first and last period occurred, number of pregnancies, birth weight and smoking.

The inclusion criteria involved the occurrence of menopause at least a year prior to the study, and the exclusion criteria included hormone replacement therapy and therapies affecting bone mass (selective estrogen receptor modulators, calcitonin, bisphosphonates, heparin steroids, thyroid hormones, antiepileptic drugs, GnRH analogue, tibolone). Other exclusion criteria were bilateral ovariectomy, endocrine and metabolic disorders, cancer, kidney and autoimmune diseases.

Analysis of gene COL1A1 polymorphism by PCR-RFLP

The analysis of COL1A1 gene polymorphisms was conducted in Laboratory of Experimental Pharmacogenetics at Chair and Department of Clinical Pharmacy and Biopharmacy at Poznan University of Medical Science. A commercial set QIAamp DNA Blood Mini Kit (Qiagen, USA) was used to isolate peripheral blood leukocyte DNA. Primer sequences for PCR and the length of PCR products were presented in Table II.

To analyze Sp1 +1245G>T and -1997G>T COL1A1 polymorphisms *Msc*I and *EcoR31*I restriction enzymes were used (Table III).

The products of PCR-RFLP reaction was subjected to electrophoretic separation in 2.75% agarose gel. Visualization after the separation with 70 V during 1.5 hours was performed using ethidium bromide. The analysis of digestion products was performed by visualization in the UV light, using documentation and computer image analysis system UVI-KS4000/Image PC (Syngen Biotech Molecular Biology Instruments).

The study also evaluated the association between COL1A1 polymorphisms and T-score, Z-score, BMI as well as L2-L4AM, L2-L4YA, L2-L4BMD values.

Statistical analysis of the obtained results was performed using SPSS 17.0 PL program. Single-factor analysis of variance (ANOVA) was used to analyze the data. Value of $p<0.05$ was considered statistically significant.

Table I. Demographic and clinical data of the studied population.

Demographic and clinical data	
Age - women at the postmenopausal age; mean ± SD	58.5±5.9
Age - women at the reproductive age; mean ± SD	31.0±4.4
Weight - women at the postmenopausal age; mean ± SD	67.0±11.8
Weight - women at the reproductive age; mean ± SD	61.9±11.0
Area of living, n (%)	**538 (100.0)**
Urban (%)	55.0
Rural (%)	45.0
Formal education, number of years, n (%)	**538 (100.0)**
Primary education (%)	1.2
Vocational education (%)	5.0
Secondary school certificate (%)	15.0
Licentiate (%)	9.5
Higher education (%)	69.3
Number of children, mean ± SD	1.6±1.1
Nutritional diet knowledge score, n (%)	**538 (100.0)**
Vegetarian (%)	3.1
Meat diet (%)	0.6
Standard (%)	84.5
Other (%)	11.8
Smoking, n (%)	**538 (100.0)**
Yes (%)	48.4
No (%)	51.6

Results

The analysis of Sp1 +1245G>T and -1997G>T polymorphisms in COL1A1 gene in postmenopausal women with osteoporosis, osteopenia and normal T-score value as well as healthy women in reproductive age showed no statistically significant differences between investigated groups. The frequency of genotypes for both polymorphisms in all groups of women followed Hardy-Weinberg equilibrium.

Analyzing Sp1 +1245G>T COL1A1 polymorphism it was observed the similar frequency of wild homozygous SS genotype in the group of osteoporosis (73.3%), in women with cerrect T-score values (69.7%), suffering from osteopenia (65.6%), and in women in reproductive age SS genotype is more frequent (71.2%) (ns). The mutated ss genotype occurs in similar frequency in women with correct T-score values (7.1%), in women with disease: osteopenia (5.5%) and in women in reproductive age (3.0%) (ns). Only in osteoporosis group the frequency was lower (1.1%) but presented only in 1 person [Table IV].

The same observation was noted regarding the -1997G>T COL1A1 polymorphism. The homozygous GG genotype was similar frequent in women with correct T-score values (64.3%), women in reproductive age (66.9%), with osteopenia (52.2%) and osteoporosis (58.9%) (ns). In postmenopausal women (with osteopenia, osteoporosis and with correct T-score values) mutated TT genotype also appeared in similar frequency (ns) [Table V].

In the group of postmenopausal women the correlation between osteopenia and osteoporosis and age (p=0.009), birth weight (p=0.005), age of last period occurrence (p=0.004), height (p<0.0001), body weight (p<0.0001) and BMI (p=0.001) has been found. The BMD L2-L4 (p<0.0001), T-score (p<0.0001), Z-score (p=0.026) values also were statistically significant different between analysed groups of postmenopausal women [Table VI].

Clinical parameters in all groups of studied women did not show any statistically significant correlation with Sp1 COL1A1 +1245G>T polymorphism. The interesting fact was the observation that osteoporotic women with homozygous ss genotype had the highest BMI value (26.7) compared to women with Ss and SS genotypes (23.7 vs. 23.5 respectively, ns). In osteoporotic women the longer reproductive period 40 years (age of last menstrual period at 52 years), compared to women with genotypes Ss - 35.7 years (age of last menstrual period at

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Table II. Primer sequences for PCR and the length of PCR products.

Amplified gene	*Primer sequence*	*The length of amplification product*
COL1A1 +1245G>T Sp1	F5'- TAA CTT CTG GAC TAT TTG CGG ACT TTT TGG-3' R5'- ATG TCC AGC CCT CAT CCT GGC C-3'	262 pz
COL1A1 -1997G>T	F5'- CAC CCT GCC CTA GAC CAC-3' R5'- CAG CAA TGG AGG GAT GGA CC-3'	257 pz

Table III. The sequences and restriction sites of Msc I and EcoR31I enzymes.

Enzyme (polymorphism)	*Recognized sequence*	*Character of hydrolysis*	*The size of obtained fragments*
*Msc*I COL1A1 +1245G/T Sp1	5'...T G G^C C A...3' 3'...A C C^G G T...5'	Enzyme hydrolizes, when T is present, and doesn't when G	GG (262pz) GT (262pz, 242pz, 20pz) TT (242pz, 20pz)
*EcoR31*I COL1A1 -1997G/T	5'…GT Y↓R AC…3' 3'…CA Y↑R TG…5' Y=C lub T, R=G lub A	Enzyme hydrolizes, when G is present, and doesn't when T	TT (257pz) GT (257pz, 176pz, 81pz) GG (176pz, 81pz)

47.6 years) and SS - 35.5 years (age of last menstrual period at 48.3 years) has been observed. This observation suggested the possible protective properties of ss genotype by reducing the risk of developing osteoporosis.

Regarding the -1997G>T COL1A1 polymorphism there was any association between BMD value and polymorphic variants. In osteopenia and osteoporosis group homozygous mutated TT genotype was associated with lower BMI (ns). There was also a tendency for early menarche in women with osteoporosis and osteopenia carrying the homozygous TT genotype compared to women with GT and GG genotypes (ns).

Discussion

Osteoporosis is a multifactorial disease with strong contribution of genetic, hormonal and environmental factors. It is widely shown that postmenopausal osteoporosis is associated with age (the disease correlates with advanced age), birth body mass (lower birth weight is a contributing factor in osteopenia and osteoporosis), age of last period occurrence (the sooner last period appears, the sooner disease develops). These observations are supported by other published studies and clinical observations characterizing osteoporosis as a disease which progresses and develops with time. The known fact also is that this disease is more common among women with lower body weight and BMI, as well as is more frequent among shorter women [7, 8].

Also our study presents some interesting clinical observations. First of all statistically significant correlation between the incidence of osteoporosis and BMD value has been observed. L2-L4 BMD was correlated in statistically significant way with the incidence of disease, what indicates on the correlation of lower BMD and the higher risk of osteopenia and osteoporosis. Clinical observations confirm that birth weight has a significant impact on achieving peak body weight and BMD value in adult life [9, 10, 11].

In this study statistically significant correlation between incidence of osteoporosis and osteopenia and birth weight indicates that birth weight is a important factor influences bone tissue metabolism and determines BMD value. Women with lower birth weight were at higher risk of osteopenia and osteoporosis when compared to women with higher birth weight.

In our study the age of last menses was also correlated statistically significant with osteoporosis. The disease was more common among women whose last menses appeared before the age of 50 years. Additionally, similarly to others clinical studies [12, 13, 14] we have demonstrated that the incidence of osteoporosis was correlated with body weight of investigated postmenopausal women (disease occurred more frequently in women with lower body weight), height (the disease was more common in shorter women) and BMI value (illness occurred more frequently in women with a lower BMI).

There are many studies searching for COL1A1 gene allelic variants and their association with osteoporosis development [15, 16, 17, 18, 19, 20, 21, 22, 23]. The frequency of the Sp1 +1245G>T COL1A1 polymorphism in osteoporotic women were also studied in many research centres. The meta-analysis of 26 studies regarding the association between Sp1 +1245G>T COL1A1 polymorphism, BMD and osteoporotic fracture showed that BMD in the lumbar spine and the femoral neck was lower in Ss heterozygotes and ss homozygotes than in homozygotes SS suggesting the s allele as a risk factor for osteoporosis development [24]. Other authors also showed that Sp1 1245G>T COL1A1 polymorphism was associated with lower BMD value and the osteoporosis incidence [15, 20, 22, 23].

In our study there was no statistically significant difference between the Sp1 +1245G>T COL1A1 polymorphism of the studied polymorphism in the group of patients with osteopenia, osteoporosis and in women with correct T-score value when compared to control group.

Table IV. The frequency of genotypes and alleles of SP1 +1245G>T COL1A1 polymorphism in women before menopause and after menopause.

COL1A1 +1245G/T	Postmenopausal women								Women with correct T-score in reproductive age	
	Osteopenia		Osteoporosis		Correct T-score		Total			
Genotypes	Observed n (%)	Expected %	Observed n (%)	Expected %	Observed n (%)	Expected %	Observed n (%)	Expected %	Observed n (%)	Expected %
SS	59 (65.6)	64.0	66 (73.3)	74.2	39 (69.7)	66.0	164 (69.5)	68.2	215 (71.2)	70.7
Ss	26 (28.9)	32.0	23(25.6)	23.9	13 (23.2)	30.5	62 (26.3)	28.8	78 (25.8)	26.8
ss	5 (5.5)	4.0	1 (1.1)	1.9	4 (7.1)	3.5	10 (4.2)	3.0	9 (3.0)	2.5
Total	90 (100.0)	100.0	90 (100.0)	100.0	56 (100.0)	100.0	236 (100.0)	100.0	302 (100.0)	100.0
Alleles										
S	144 (80.0)	-	155 (86.1)	-	91 (81.3)	-	390 (82.6)	-	508 (84.1)	-
s	36 (20.0)	-	25 (13.9)	-	21 (18.7)	-	82 (17.4)	-	96 (15.9)	-
Total	180 (100.0)	-	180 (100.0)	-	112 (100.0)	-	472 (100.0)	-	604 (100.0)	-

Table V. The frequency of genotypes and alleles of -1997G>T polymorphism in women before menopause and after menopause.

COL1A1 -1997G>T	Postmenopausal women								Women with correct T-score in reproductive age	
	Osteopenia		Osteoporosis		Correct T-score		Total			
Genotypes	Observed n (%)	Expected %	Observed n (%)	Expected %	Observed n (%)	Expected %	Observed n (%)	Expected %	Observed n (%)	Expected %
GG	47 (52.2)	55.4	53 (58.9)	62.2	36 (64.3)	63.2	136 (57.6)	59.8	202 (66.9)	67.2
GT	40 (44.4)	38.1	36 (40.0)	33.3	17 (30.4)	32.6	93 (39.4)	35.1	91 (30.1)	29.6
TT	3 (3.4)	6.5	1 (1.1)	4.5	3(5.3)	4.2	7 (3.0)	5.1	9 (3.0)	3.2
Total	90 (100.0)	100.0	90 (100.0)	100.0	56 (100.0)	100.0	538 (100.0)	100.0	302 (100.0)	100.0
Alleles										
G	134 (74.4)	-	142 (78.9)	-	89 (79.5)	-	365 (77.3)	-	495 (81.9)	-
T	46 (25.6)	-	38 (21.1)	-	23 (20.5)	-	107 (22.7)	-	109 (18.1)	-
Total	180 (100.0)	-	180 (100.0)	-	12 (100.0)	-	472 (100.0)	-	604 (100.0)	-

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Tabela VI. Investigated parameter in postmenopausal women with osteopenia, osteoporosis and correct T-score.

Parameter	Group of women	n	Mean	±SD	Min	Max	p
T-score	osteopenia	90	-1,8354	,4139	-2,47	-1,14	0,000
	osteoporosis	90	-3,1662	,5524	-4,73	-2,50	
	correct T-score	56	,1395	,9667	-,97	3,13	
	Total	236	-1,8743	1,4161	-4,73	3,13	
Z-score	osteopenia	90	-,8039	,5916	-1,97	,77	0,026
	osteoporosis	90	-3,0324	13,3367	-128,00	,98	
	correct T-score	56	,6445	1,0306	-1,85	2,65	
	Total	236	-1,3101	8,3599	-128,00	2,65	
Age [years]	osteopenia	90	54,4	7,8	31,0	77,0	0,009
	osteoporosis	90	57,6	7,9	37,0	78,0	
	correct T-score	56	53,9	8,5	28,0	71,0	
	Total	236	55,5	8,2	28,0	78,0	
Birth body mass [g]	osteopenia	26	3216,2	400,6	2500,0	4500,0	0,005
	osteoporosis	16	3141,3	536,3	2470,0	4500,0	
	correct T-score	18	3633,3	494,3	2460,0	5100,0	
	Total	60	3321,3	504,9	2460,0	5100,0	
Age of first menses occurence [years]	osteopenia	90	13,2	2,2	9,0	18,0	0,942
	osteoporosis	90	13,2	2,1	9,0	18,0	
	correct T-score	56	13,3	2,2	3,0	16,0	
	Total	236	13,2	2,2	3,0	18,0	
Age of last menses occurence [years]	osteopenia	90	49,7	4,3	38,0	60,0	0,004
	osteoporosis	90	48,2	4,8	34,0	58,0	
	correct T-score	56	50,6	3,7	41,0	58,0	
	Total	236	49,3	4,5	34,0	60,0	
Reproduction years	osteopenia	90	36,4	4,8	23,0	49,0	0,177
	osteoporosis	90	35,6	4,8	24,0	47,0	
	correct T-score	56	37,1	4,6	27,0	48,0	
	Total	236	36,3	4,8	23,0	49,0	
Years after last menses	osteopenia	90	8,6	5,8	,0	25,0	0,094
	osteoporosis	90	10,3	5,2	1,0	22,0	
	correct T-score	56	8,9	5,3	1,0	23,0	
	Total	236	9,3	5,5	,0	25,0	
Number of pregnancies	osteopenia	90	1,9	1,1	,0	6,0	0,889
	osteoporosis	90	1,9	1,3	,0	7,0	
	correct T-score	56	1,9	1,3	,0	6,0	
	Total	236	1,9	1,2	,0	7,0	
Body mass (kg)	osteopenia	90	65,2	9,6	41,0	90,0	0,000
	osteoporosis	90	60,9	9,1	43,0	85,0	
	correct T-score	56	68,9	12,4	50,0	100,0	
	Total	236	64,4	10,6	41,0	100,0	
Height [cm]	osteopenia	90	162,8	4,8	153,0	175,0	0,000
	osteoporosis	90	159,9	5,2	150,0	175,0	
	correct T-score	56	163,1	5,8	152,0	176,0	
	Total	236	161,8	5,4	150,0	176,0	

Tabela VI (cd). Investigated parameter in postmenopausal women with osteopenia, osteoporosis and correct T-score.

Parameter	Group of women	n	Mean	±SD	Min	Max	p
BMI [kg/m2]	osteopenia	90	24,6	3,3	17,3	34,3	0,001
	osteoporosis	90	23,6	3,1	17,1	31,6	
	correct T-score	56	25,9	4,7	18,3	37,2	
	Total	236	24,6	3,7	17,1	37,2	
BMD L2-L4 [g/cm3]	osteopenia	90	,9733	,0499	,90	1,07	0,000
	osteoporosis	90	,8178	,0715	,63	,90	
	correct T-score	56	1,2204	,1046	1,08	1,47	
	Total	236	,9726	,1710	,63	1,47	
BMD L2-L4 YA	osteopenia	90	81,1444	4,1935	75,0	89,0	0,000
	osteoporosis	90	68,2556	5,7914	53,0	75,0	
	correct T-score	56	102,1250	9,0193	90,0	123,0	
	Total	236	81,2076	14,3845	53,0	123,0	
BMD L2-L4 [AM/%]	osteopenia	90	89,5444	6,6690	76,0	108,0	0,000
	osteoporosis	90	78,6222	7,7613	60,0	92,0	
	correct T-score	56	110,5000	10,7788	92,0	133,0	
	Total	236	90,3517	14,7149	60,0	133,0	

Much less is known about the -1997G>T COL1A1 variant located in promoter region. In postmenopausal Spanish women (n=256) the statistically significant association between this polymorphism and BMD values in the lumbar spine has been noted. This polymorphism is also considered to be a very important cis-regulatory element in *in vivo* regulation of transcription [25].

Analysis of published studies focus on association between -1997G>T COL1A1 polymorphism and bone parameters, risk of bone fracture and the incidence of osteoporosis shows that some differences in investigated populations. Several studies showed that homozygous TT genotype and T allele were associated with lower BMD value [26, 27, 28]. Gender specific analysis performed by Jin et al. showed associations between the promoter polymorphisms and osteoporosis-related phenotypes where L2-L4 BMD values were 0.06 units lower in female GG homozygotes as compared with GT heterozygotes (p=0.02) [6]. This comparison was also present is other studies [27, 29, 30, 31]. Similar results were obtained with regard to femoral neck although they lacked statistical significance. The association of GG genotype with lower BMD values was also observed in a study by made Selezneva et al. [32].

However, it needs to be underlie that the obtained results could be different depending of the ethnic group or chosen population. It is also worth noting that the obtained effect resulting from one or even a couple of polymorphisms is very small in a polygenic disease such as osteoporosis and does not give clear answers regarding possible prevention or diagnosis.

Conclusions

An evaluation of Sp1 +1245G>T (rs1800012) and -1997G>T (rs 1107946) COL1A1 polymorphisms showed any influence of these genetic variants on osteoporosis development in Polish postmenopausal women. The presented correlation between osteoporosis and age, birth weight, age of last menses occurrence, height, body weight and BMI value confirms the important role of environmental factors in disease etiology.

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