IMPLICATION OF GENETIC FACTORS IN OSTEOPOROSIS SUSCEPTIBILITY

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Abstract. Osteoporosis is a multifactorial disease characterized by a decrease in bone mass and deterioration of bone architecture. Genetic factors are determinants of peak bone mass and may influence age-related decreases of bone mass. WHO has established an operational criterion based on bone density measuring, the T-score. 122 cases were studied, 51 diagnosed with primary osteoporosis. Mean age was 57.6 years. The main inclusion criterion was the acceptance of affected individuals to participate in the study. Accurate family history was taken. Daughters of affected persons were evaluated by DEXA technique. 67.2% of them had T-score values that indicated osteopenia or osteoporosis (mean value -2.3SD). In conclusion, descendents of affected parents are at a high risk for osteoporosis, important aspect for primary prevention.

Keywords: osteoporosis, T-score, family history

INTRODUCTION

Osteoporosis is one of the major and growing health care problems around the world, largely related to the general aging of societies, with improvement in public and preventive health and delay in mortality. Osteoporosis is a multifactorial disease characterized by a decrease in bone mass and deterioration of bone architecture [11]. Genetic factors are determinants of peak bone mass and may influence age-related decreases of bone mass [7]. Predisposition to osteoporosis is genetically determined, several genes, each with a small effect, being involved.

Those with a family history of fracture or osteoporosis are at an increased risk; the heritability of the fracture as well as low bone mineral density are relatively high, ranging from 25 to 80 percent. There are at least 30 genes associated with the development of osteoporosis [14]. The magnitude of individual genetic effects differs in different population subsets and in different environments. The heritability of bone density, measured by a several methods in twin studies and inter-generational studies, has been shown to be very high. There is a strong correlation for fracture risk between mothers and daughters and also between maternal grandmothers and daughters, suggesting there is a shared component, either genetic or environmental, which influences bone fragility. Those who have already had a fracture are at least twice as likely to have another fracture compared to someone of the same age and sex [12].

WHO has established an operational criterion based on bone density measuring, the T-score [9, 10].

OBJECTIVE

The objective of the present study was to describe genetic epidemiologic aspects of osteoporosis, as genetic and familial factors may predict the disease risk in otherwise healthy peri- and post-menopausal women. Since osteoporosis is easier to prevent than to treat, the goal is therefore to identify individuals who might be at high risk.

MATERIALS AND METHODS

122 cases were studied, 51 diagnosed with primary osteoporosis. Mean age was 57.6 years. The main inclusion criterion was the acceptance of affected individuals to participate in the study. Accurate family history was taken. Daughters of affected persons were evaluated by DEXA technique.

Dual energy x-ray absorptiometry scan (DXA, formerly known as DEXA) for diagnosing osteoporosis. DXA measures bone density in the hip and the spine. The bone density of the subject is then compared to the average peak bone density of young adults of same sex and race. This score is called the "T score," and it expresses the bone density in terms of the number of standard deviations (SD) below peak young adult bone mass. Osteoporosis is defined as bone density T score of –2.5 SD or below [9, 10].

Distribution of the cases in the study lots:

LOT I- 62 cases with mean age of 51±3.98, just before or soon after menopause: mean 100.04 months±33.43.

LOT II-60 cases with mean age of 64.39±5.64, had been in menopause for about 209.35 ±75.94 months

RESULTS AND DISCUSSIONS

Osteoporosis is a disease of bone that leads to an increased risk of fracture. In osteoporosis the bone mineral density (BMD) is reduced, bone microarchitecture is disrupted, and the amount and variety of non-collagenous proteins in bone is altered [14]. Family history of osteoporosis, for example, having a mother with an osteoporotic hip fracture doubles your risk of hip fracture [11, 15].

2/3 of the women who had mothers with osteoporosis developed this disease too, which proves that the maternal parent with osteoporosis is a high risk factor, unfortunately not possible to influence (**Table 1, Fig. 1**).

Osteoporosis was developed in more than 2/3 of the cases in which menopause was settled before the age of 45.From the cases that had 2.11 risk factors, 70% of the cases were diagnosed with osteoporosis (**Table 2, Fig. 2**).

Table 1. Representation of risk factor-Mother with O.P.-according to T score

T SCORE/ Risk factors	Mother with O.P. TOTAL LOT	LOT I	LOT II
NORMAL	10 (32.7%)	8 (42%)	2 (20%)
OSTEOPOROSIS	19 (67.2%)	11 (58%)	8 (80%)
Osteopenia	7 (36,8%)	4 (36,3%)	3 (37,5%)
Vertebral osteoporosis	7 (36,8%)	4 (36,3%)	3 (37,5%)
General osteoporosis	5 (26,3%)	3 (27,2%)	2 (25%)
TOTAL	29	19	10

67.2% of cases had T-score values that indicated osteopenia or osteoporosis (mean value -2.3SD).
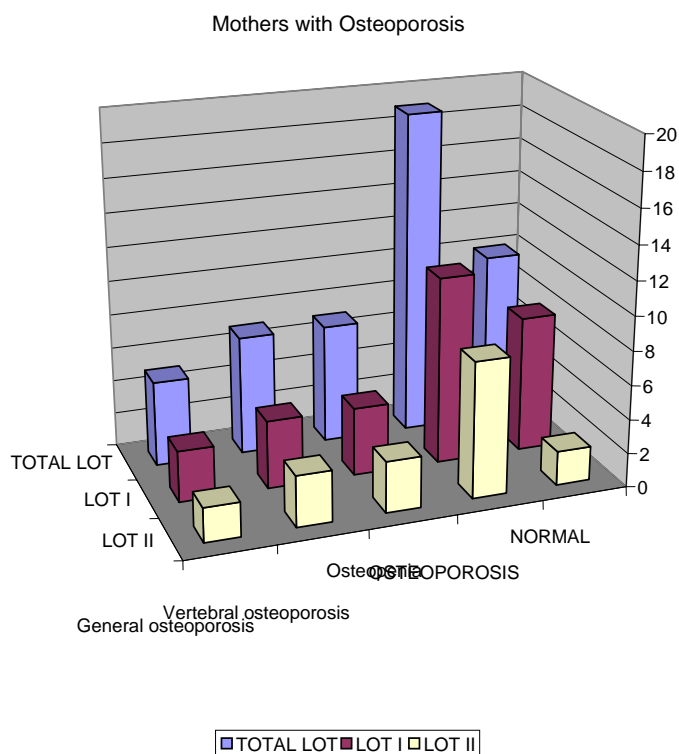
Mothers with Osteoporosis

Figure 1. Mothers with Osteoporosis graph

Table 2. Representation of risk factor – Menopause before 45 ys.–according to T score

T Score	Menopause before 45 TOTAL LOT	LOT I	LOT II
NORMAL	9 (31.4%)	6 (26%)	3 (23%)
OSTEOPOROSIS	30 (68.6%)	17 (74%)	13 (77%)
Osteopenia	10 (33,3%)	6 (35,3%)	4 (30,7%)
Vertebral osteoporosis	12 (40%)	6 (35,3%)	6 (46,1%)
General osteoporosis	8 (26,6%)	5 (29,4%)	3 (23%)
TOTAL	39	23	13

Cases of menopause before 45 y.o.
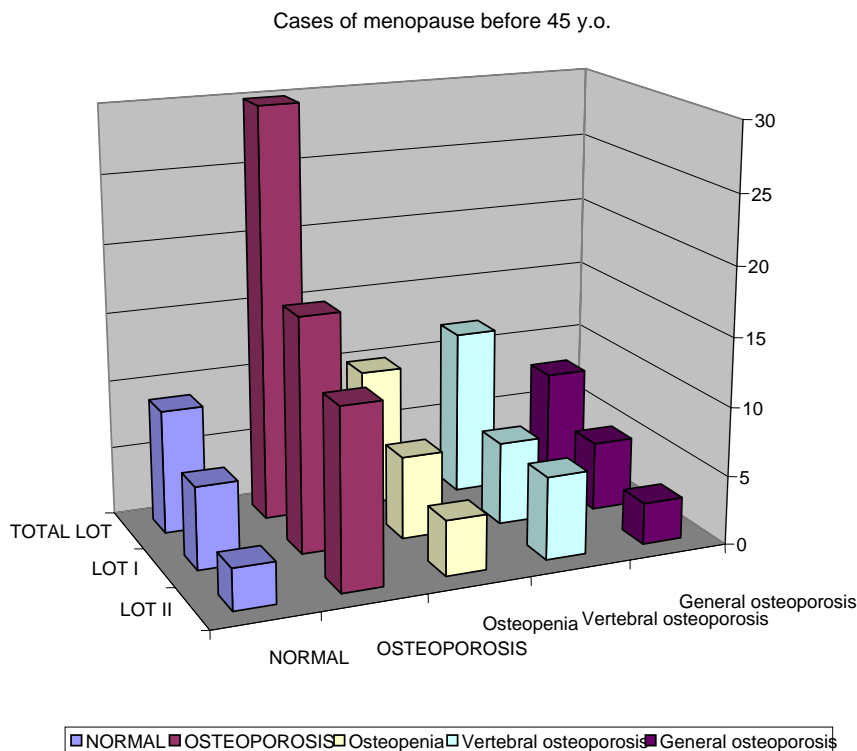
Figure 2. Cases of menopause before 45 y.o. graph

Table 3. Vertebral fractures

WHO category	Age 50-64	Age > 64	Overall
Normal	6.4%	10.5%	8.9%
Osteopenia	7.4%	17.8%	12.3%
Osteoporosis	27.8%	49.7%	49.2%

Grouping the risk factors on categories, we certified once again that in the presence of risk factors, osteoporosis is observed in more than ¾ of cases.

All the subjects from the survey who had the following associated risk factors had osteoporosis: mother with osteoporosis, menopause before the age of 45, underweight.

From the most to the least important risk factors, the development of osteoporosis can be influenced as follows:
- 90% underweight
- 87% autoimmune diseases, corticosteroid medication, endocrine diseases
- 77% premature menopause
- 66% track records of mother with osteoporosis, lack of sun exposure, no milk uptake, alcohol use and tobacco smoke
- 54% sedentary

Given its influence on the risk of fragility fracture, osteoporosis may significantly affect life expectancy and quality of life. Those who have already had a fracture are at least twice as likely to have another fracture compared to someone of the same age and sex [12].

Although osteoporosis cases have an increased mortality rate due to the complications of fracture, most subjects die with the disease rather than of it [8] (**Table 3**).

Hip fractures can lead to decreased mobility and an additional risk of numerous complications (such as deep venous thrombosis and/or pulmonary embolism, pneumonia). The 6-month mortality rate following hip fracture is approximately 13.5%, and a substantial proportion (almost 13%) of people who have suffered a hip fracture need total assistance to mobilize after a hip fracture [4].

Vertebral fractures, while having a smaller impact on mortality, can lead to severe chronic pain of neurogenic origin, which can be hard to control, as well as deformity [1, 3]. Though rare, multiple vertebral fractures can lead to such severe hunch back (kyphosis) that the resulting pressure on internal organs can impair one's ability to breathe [2].

Osteoporosis can be prevented with lifestyle advice and sometimes medication, and in people with osteoporosis treatment may involve lifestyle advice, preventing falls and medication [8, 13].

Rehabilitation of subjects with osteoporosis includes adequate pain management, early

mobilization, specific training of muscles and coordination, instruction on how to avoid falls, nutrition and lifestyle modifications, and psychosocial assessment [7].

The aims of the Kanis JA et all [5]study were to determine whether a parental history of any fracture or hip fracture specifically are significant risk factors for future fracture in an international setting, and to explore the effects of age, sex and bone mineral density (BMD) on this risk. The results of the different studies were merged from the weighted beta coefficients [5]. A parental history of fracture was associated with a modest but significantly increased risk of any fracture, osteoporotic fracture and hip fracture in men and women combined. The risk ratio was higher at younger ages but not significantly so. No significant difference in risk was seen between men and women with a parental history for an osteoporotic fracture Its identification on an international basis supports the use of this risk factor in case-finding strategies [6].

CONCLUSIONS

- The maternal parent with osteoporosis is a high risk factor, unfortunately not possible to influence.
- The settling of menopause before the age of 45 is a very important cause for the release of physiopathological mechanisms of osteoporosis.
- Descendents of affected parents are at a high risk for osteoporosis, important aspect for primary prevention.
- The identification of susceptibility genes for osteoporosis is expected to be a major contributing factor toward the long-term goal of understanding the molecular biology of the normal variation in bone strength and how it may be modified to prevent osteoporotic fractures.
- These results provide an initial epidemiologic profile for osteoporosis and information useful for genetic counseling.
- Bone mineral density (BMD) and clinical risk factors predict hip and other osteoporotic fractures. The combination of clinical risk factors and BMD provide higher specificity and sensitivity than either alone.
- We conclude that a parental history of osteoporotic fracture (particularly a family history of hip fracture) confers an increased risk of fracture that is independent of BMD.

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