Chapter I

Introduction

Osteoporosis is a disease of the skeleton characterized by decreased bone mass and deterioration of bone tissue architecture leading to increased bone fragility. Osteoporotic bone changes are initially silent and can progress undetected until a low trauma fraction occurs. At menopause, decreased gonadal sex steroid production normally leads to rapid bone loss. Postmenopausal osteoporosis is the most common primary type and it is a silent disease characterized by rapid bone loss in recently postmenopausal women, affecting millions of the women worldwide. The results of many studies in Saudi Arabia found the development of osteoporosis among postmenopausal Saudi females it should be considered as a matter of public health.

Osteoporosis has a complex multifactorial polygenic disease. Although there are several environmental influences on BMD, such as diet (calcium intake and alcohol consumption) and lifestyle factors (smoking and physical exercise), also a genetic contribution to the pathogenesis of osteoporosis. There are many candidate genes implicated in the determination of BMD and in the pathogenesis of osteoporosis.

Estrogens are known to play an important role in regulating bone homeostasis and preventing postmenopausal bone loss. Its deficiency after menopause is the main reason for accelerated bone loss and development of post-menopausal osteoporosis, which are preventable by estrogen administration. Decreases in estrogen levels

contribute not only to early postmenopausal bone loss but also to bone loss with aging.

In different studies, *estrogen receptor alpha* (*ERα*) gene polymorphisms have been associated with several pathologic conditions such as breast cancer, prostate cancer and osteoporosis. *ERα* is a major regulator of bone metabolism which can modulate gene expression via a "classical" pathway involving direct DNA binding to *estrogen-response elements* (*EREs*) or via "non-classical" pathways involving protein–protein interactions. The most widely studied are the two restriction fragment length polymorphisms (RFLPs) the *Pvu*II (T \C) and *Xba*I (A\G). Alleles P and X (absence of restriction sites), as well as alleles p and x (presence of restriction sites), are strongly associated with each other. Both *Pvu*II and *Xba*I RFLPs lie in the first intron of *ERα* gene have been widely associated with low BMD in many studies but not in all populations studies.

Therefore, the study aims to establish these polymorphisms (*Pvu*II and *Xba*I) as a genetic marker for osteoporosis in postmenopausal Saudi women by study the association of commonly studied polymorphisms of *ERα* with BMD and the possible effect by the frequency distribution of *ERα* genotypes in the women with osteoporosis and normal bone mass within the group to confirm or refute the association to predict diagnosis before it become development.