Osteoporosis as a Manifestation of Endocrine Diseases

Essay

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By

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بسم الله الرحمن الرحيم
وأنزل الله عليك
الكتاب والحكمة
وعلَّمَكَ مَا لَمْ تَكُن
تَعْلَمُ وكَانَ فَضْلُ
اللَّهِ عَلَيْكَ عَظِيماً
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Noha Reda Abd Elmongy

Contents

List of Abbreviations

AGHD	: GH-deficient
AN	: Anorexia nervosa
BMD	: Bone mineral density
BSAP	: Bone-specific alkaline phosphatase
BUA	: Broadband ultrasound attenuation
CaSR	: Calcium sensing receptor
cGCR	: Cytosolic glucocorticoid receptor
DEXA	: Dual-energy X-ray absorptiometry
DM	: Diabetes mellitus
DPD	: Deoxypyridinoline
ERs	: Estrogen receptors
FDA	: Food and drugs administration
FIT	: Fracture Intervention Trial
Free T4	: Hypothalamic–pituitary–thyroid
FSH	: Follicle stimulating hormone
GCs	: Exogenous glucocorticoids
GH	: Growth hormone
GHD	: Growth hormone deficient
GIO	: Glucocorticoid-induced osteoporosis
HR pQCT	: High resolution peripheral quantitative computed tomography
HR-MRI	: High-resolution magnetic resonance imaging
HRT	: Hormone replacement therapy
HT	: Hormonal therapy
IGF I	: Insulin-like growth factor I
IGF	: Insulin like growth factor-1
IL	: Interleukin
IRR	: Incidence rate ratio
ISCD	: International Society for Clinical Densitometry
LH	: Luteinizing hormone
LRP5	: Lipoprotein receptor related protein 5

List of Abbreviations *(Cont...)*

mcroCT : Microcomputed tomography
M-CSF : Amacrophage colony-stimulating factor
MRI : Magnetic Resonance Imaging
NFkB : Nuclear factor kB
NICE : National Institute of Clinical Excellence
NTX : N-telopeptide (NTX)
OC : Osteocalcin
OI : Osteogenesis imperfecta
OP : Osteoporosis
OPG : Osteoprotegerin
OST : Osteoporosis Self-assessment Tool
PBM : Peak bone mass
PD : Periodontal disease
PHPT : Primary hyperparathyroidism
PMO : Postmenopausal osteoporosis
PPAR : Peroxisome proliferator-activated receptor
PTH : Parathyroid hormone
PTH1R : Parathyroid hormone receptor-1
PVN : Paraventricular nucleus
QCT : Quantitative computed tomography
QUI : Quantitative ultrasound index
QUS : Quantitative ultrasonography
RANK : Receptor activator of NF KB
RANKL : Receptor activator of nuclear factor-κ B-ligand
SAXS : Small Angle X ray Scattering
SERMs : Selective estrogen receptor modulators
SNPs : Single nucleotide polymorphisms
SOS : Speed of sound
SOST : Sclerostin
STAT : Signal transducers and activators of transcription

List of Abbreviations *(Cont...)*

T_3	: Triiodothyronine
T_4	: Tetraiodothyronine
TGFb	: Transforming growth factor b
TNF-alfa	: Tumor necrosis factor alfa
TRAIL	: Tumor necrosis factor-related apoptosis-inducing ligand
TRH	: Thyrotrophin-releasing hormone
TRs	: Thyroid receptors
TSH	: Thyroid stimulating hormone
TSHR	: TSH receptor
ucOC	: Undercarboxylated osteocalcin
vBMD	: volumetric BMD
µCT	: Micro-CT
3-D	: Three-dimensional

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Introduction

Osteoporosis, defined as a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture, is a major public health problem throughout the world. Elderly people are the fastest growing population in the world and, as people age, bone mass declines and the risk of fractures increases ***(Lane, 2006).***

This disease is considered a "silent thief" that generally does not become clinically apparent until a fracture occurs. Osteoporosis represents an increasingly serious problem in the United States and around the world. Many individuals, male and female, experience pain, disability, and diminished quality of life as a result of having this condition. The economic burden the disease imposes is already considerable and will only grow as the population ages ***(Ahmed and Elmantaser, 2009).***

Osteoporosis has been divided into several classifications according to etiology and localization in the skeleton. Osteoporosis is initially divided into localized and generalized categories. These two main categories are classified further into primary and secondary osteoporosis ***(Orwoll et al., 2008).***

Variations in the alimentary and endocrine systems in both women and men have a fundamental role in the development of osteoporosis: if these variations are combined with an inappropriate life style (eg, inadequate physical exercise, alcohol

abuse or smoking), pathologies such as hyperparathyroidism, thyrotoxicosis and/ or the use of drugs such as antipsychotics or corticosteroids, the risk of osteoporosis is increased ***(Lanzini et al., 2006).***

Osteopenia and osteoporosis are among the complications of Diabetes mellitus (DM) as it may alter bone remodeling. Moreover, DM increases the risk and severity of chronic inflammatory periodontal disease, in which bone resorption occurs ***(Gracia-Hernandez et al., 2012).***

Thyroid diseases have widespread systemic manifestations including their effect on bone metabolism. On one hand, the effects of thyrotoxicosis including subclinical disease have received wide attention from researchers over the last century as it an important cause of secondary osteoporosis. On the other hand, hypothyroidism has received lesser attention as its effect on bone mineral metabolism is minimal ***(Dhanwal, 2011).***

Exogenous glucocorticoids (GCs) are used as anti-inflammatory and immunosuppressive drugs in the treatment of a wide range of rheumatic and other inflammatory diseases. However, their pleiotropic effects may lead to numerous adverse effects such as unwanted metabolic effects and osteoporosis ***(Strehl et al., 2011).***

The presence of osteoporosis in men is correlated mainly with the effect of growth hormone (GH) and hypogonadism. GH stimulates the increase in muscle mass and the formation of

bone tissue. It was stated that GH replacement improves target organ sensitivity to parathyroid hormone (PTH), PTH circadian rhythm, calcium and phosphate metabolism, bone turnover, and bone mineral density (BMD) in adult GH-deficient (AGHD) patients. In postmenopausal women with established osteoporosis, GH and insulin like growth factor-1 (IGF-1) concentrations are low, and administration of GH has been shown to increase bone turnover and BMD, but the mechanisms remain unclear ***(Joseph et al., 2008).***

Aim of the Work

The aim of this review is to discuss the update in the causes and pathogeneses of osteoporosis associated with endocrinal disorders.

Osteoporosis

Definition:

Osteoporosis is an asymptomatic systemic disease characterized by deterioration of the microarchitecture of bone and low bone mass, which ultimately predisposes patients to fractures secondary to low-energy mechanisms ***(McKean et al., 2013).*** Osteoporosis takes place when bone resorption by osteoclasts far exceeds bone formation by osteoblasts ***(Muhammad et al., 2012).***

Osteoporosis remains a major public health problem through its association with fragility fractures. Despite the availability of preventative therapeutic agents, the incidence and its associated costs continue to rise globally. Understanding osteoporosis epidemiology is essential to developing strategies to reduce the burden of osteoporotic fracture in the population ***(Cole et al., 2008).***

Osteoporotic fractures are associated with increased mortality and major morbidity, including loss of independence, reduced function and mobility, pain, kyphosis and respiratory compromise ***(Walsh & Eastell, 2013).***

Epidemiology

It is a common disease affecting 8 million women and 2 million men in the United States and leading to more than 2 million osteoporotic fractures annually ***(Diab and Watts, 2013).***

About half of the women at age of 50 or older will suffer an osteoporotic fracture during their lifetime, causing disability, increased mortality, and financial burden, Fragility fractures occur less commonly in men, but they are associated with a higher mortality than in women ***(Mazziotti et al., 2012).***

The social and economic burden of osteoporosis is increasing steadily because of the aging of the world population. Currently affecting more than 10 million people in the United States, osteoporosis is projected to impact approximately 14 million adults over the age of 50 by the year 2020 ***(Lane, 2006).***

Epidemiological studies have recently reported on the burden of hip and vertebral fractures in Mexico. It is estimated that 1 in 12 Mexican women and 1 in20Mexican men will have a hip fracture after the age of 50 (lifetime risk probability of 8.5 and 3.8%, respectively) Compared to other countries, Mexico shows intermediate hip fracture incidence rates12 (age-standardized incidence rates of 203 and108 per 100, 000 person years in women and men, respectively) ***(Clark et al., 2013).***

During early adult life there are actually more fractures in men than women; most of these fractures are traumatic. After the menopause, women have an increasingly greater risk of osteoporotic fracture. This increased risk is related to the dramatic loss of estrogen with the cessation of menses. In men, there is analogous dramatic decrease in androgen secretion ***(Adler, 2013).***