

Introduction

Menopause is defined as a cessation of ovarian function that results in permanent amenorrhea. Because 12 months of amenorrhea ensures a cessation of ovulation in older women, definitive diagnosis is usually made retrospectively. A standardized system for the chronology and terminology of menopause was developed by a consensus panel in 2001. They defined the *menopausal transition* as the period of time from the first variation in menstrual cycle length and elevated follicle-stimulating hormone (FSH) to the final menses. *Menopause* is the year of amenorrhea after the final period. *Perimenopause* includes the transition phase and menopause itself. *Postmenopause* includes the remaining lifetime after menopause (Soules et al., 2001).

Menopause, whether it occurs naturally or surgically, is characterized by the loss of hormones produced by the ovaries. In natural menopause, ovarian function decreases slowly over several years until menstruation ceases, but in surgical menopause circulating levels of estrogen, progesterone and androgen decrease abruptly. It is controversial whether prophylactic bilateral oophorectomy

at the time of hysterectomy is beneficial or harmful in premenopausal women (**Suna et al., 2009**).

The WHO definition of osteoporosis in women is based on a BMD value 2.5 standard deviation (SD) or more below the mean for young normal white women. Bone loss is progressive and is not associated with symptoms until a fracture occurs – the main clinical feature of osteoporosis. According to the WHO, fractures are "caused by injury that would be insufficient to fracture normal bone". In other words, a fragility fracture can result from minor trauma, such as a fall from a standing height or less. The International Osteoporosis Foundation (IOF) estimates that 200 million women suffer from osteoporosis across the world. Moreover, osteoporosis has been misconceived as a women's disease because it also affects men significantly. Indeed, at least one in five men compared to one in three women over the age of 50 will have an osteoporosis-related fracture in their remaining lifetime (**Maalouf et al., 2007**).

A bone mineral density measurement using dual energy X-ray absorptiometry has been the "gold-standard" for diagnosing osteoporosis and evaluating fracture risk. Although DXA has proven to be a reliable predictor of future fracture, its high cost and its limited availability precludes its wide application in remote areas. Quantitative ultrasound of bone is an inexpensive, radiation-free method

that provides information on fracture risk, and perhaps bone quality. It can be used to assess the risk of fractures at the spine, hip and non-vertebral sites. Cut-off values of T-Score for the heel could be considered -1 SD (**Maalouf et al., 2007**).

Several specific questionnaires have been developed to measure Quality of Life (QOL) in osteoporosis. The most widely used are the Osteoporosis Quality of Life Questionnaire (OQLQ), the Osteoporosis Assessment Questionnaire (OPAQ), the Osteoporosis-Targeted Quality of Life Questionnaire (OPTQoL), and the Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO). However their length and administration time have limited their use to clinical trials. For this reason, specific short form questionnaires, such as the mini-OQLQ and the ECOS-16 (Assessment of health-related quality of life in osteoporosis), have been developed (**Abourazzak et al., 2009**).

Mammography refers to the process of obtaining images of the breast using low-energy x-rays. A typical mammographic machine generates low-energy [25-30 kilovolt peak (kVp)] x-rays using a small (0.3 mm) focal spot source, typically molybdenum. Dark areas on

mammogram represent areas with minimal absorption (fat), whereas white areas represent moderate absorption by fibroglandular tissue or extensive absorption by calcium salts. Image quality is affected by a sum of factors, including breast tissue density, compressed thickness, positioning, motion, and radiation dose which was limited by the Food and Drug Administration (FDA) to 300 mrad for an average thickness breast per exposure (**Mark et al., 2004**).

Aim of the Work

The aim of this work was to find out if there was a correlation between mammographic breast density and bone mineral density in menopausal women (either naturally or surgically) in comparison to control normal cases.

Menopause

Definition:

Menopause, from the Greek ‘Menos’ (month) and ‘Pausis’ (cessation), is defined as the last menstrual period. The diagnosis can only be made retrospectively after a minimum of 1 year’s amenorrhea. **(Edmonds et al., 2007 and Michele, 2007)**. It occurs at a mean age of 51 years. Despite a great increase in the life expectancy of women, the age at menopause has remained remarkably constant. **(Shifren and Schiff, 2007)**. The physiological changes which result in the final menstrual period (FMP) can start 10 years prior to this. This episode of dynamic neuroendocrine change is characterized by ‘the climacteric’ from the Greek ‘Klimax’ ladder, that is, the climb to the menopause. **(Edmonds et al., 2007 and Lauren and Howard, 2007)**.

The age at menopause appears to be genetically determined and is unaffected by race, socioeconomic status, age at menarche, or number of prior ovulations. Factors that are toxic to the ovary often result in an earlier age of menopause; women who smoke experience an

earlier menopause, as do many women exposed to chemotherapy or pelvic radiation. (**Shifren and Schiff, 2007**)

About 20% of women will complain of symptoms that they associate with the menopause. (**Rees et al., 2005**)

Epidemiology:

The average age of menopause in the United States is 49–50 years, and it relates to health and genetic background (**Pernoll, 2001 and Lauren and Howard, 2007**).

About half of all women of America will go through menopause before age 51 and the rest will go through it after. Most women will finish menopause between the ages of 42 and 58 (**Lauren and Howard, 2007**).

The age of menopause is not correlated with age at menarche, height, weight, parity, or prolonged use of oral contraceptives. **Early menopause** has been associated with smoking, infection, chemotherapy (especially alkylating agents), radiation, surgical procedures that impair ovarian blood supply, tumors, or surgical removal of the ovaries. Early menopause has even been related to left-handedness,

although menopause is not classified as being premature unless menses cease at ≤ 35 y of age. (**Pernoll, 2001**).

Seventy percent of Caucasians and Afro-Caribbeans suffer from hot flushes and sweats (the commonest menopausal symptoms). This compares to 10–20% of Japanese and Chinese women and may reflect cultural differences or may be diet related (e.g. isoflavone consumption in Asia) (**Edmonds, 2007**).

Cessation of menstruation and the development of climacteric symptoms and complaints can occur as early as a few years after menarche. The reasons for premature ovarian failure are unknown. Although 0.9% of women in the United States may experience it before age of 40 (**Lauren and Howard, 2007**).

The mean age at natural menopause was 46.70 ± 5.44 years. Earlier menopause occurred in women living in semiurban areas, divorced/separated and less educated women, and women who were younger at: first marriage, widowhood, divorce/separation and first or last full-term pregnancy. Later menopause occurred in women who had: irregular menstrual periods before 25 years, dysmenorrhoea and mid-cycle spotting (**Hidayet et al., 1999**).

The incidence of menopause-associated symptoms in Egyptian women is higher than in the West, probably because of the different ‘sociocultural attitudes’ towards the menopause in different communities. Bone mineral density charts have been constructed for Egyptian women and show that, in general, they have a lower bone mineral density compared to their Western counterparts. After the menopause, they suffer from osteoporosis, particularly at the femoral neck. Egyptian women do not know much about the menopause, except that the incidence of osteoporosis is increased. Their attitude towards the menopause is generally positive and about one-third of them regard the menopause as ‘a normal physiological change’. Nevertheless, there exists a need for an awareness campaign in order to educate them about this important stage of their lives (**Sallam et al., 2006**).

Pathophysiology:

It may be associated with distressing clinical problems such as reduced fertility, menstrual irregularity and vasomotor symptoms. The intermediate sequelae of these changes are typically seen in the skin and urogenital

tract and in the long term, in skeletal and cardiovascular pathology (**Edmonds, 2007**).

The physiology of the climacteric requires a brief review of ovarian physiology. Primordial germ cells migrate to the genital ridge by 5 weeks of gestation. Successive mitotic cellular divisions form oogonia, which in turn give rise to oocytes. Although there are approximately 7 million oogonia present in the fetus at 20 weeks of gestation, their numbers gradually decline, leaving 2 million at birth and only 300,000 at puberty. This reduction continues until menopause. This decline is due to atresia (as a primary cause of loss) and ovulation (400–500 per lifetime). (**Pernoll, 2001**).

Estrogen and progesterone materially decreases at, or before, the time of menopause as well as when the ovaries are removed or sufficiently altered to cease physiologic functioning. Growth hormone (GH) and dehydroepiandrosterone sulfate (DHEA) also decrease at menopause. Whereas the latter hormones undoubtedly have importance, investigation of the impact of hormonal replacement of GH and DHEAS is just beginning. (Table 1) (**Pernoll, 2001**).

Table (1): Mean Serum Concentrations of Hormones in Premenopausal and Postmenopausal Women (Pernoll, 2001).

	Premenopausal (ng/mL)	Postmenopausal (ng/mL)
Androstenedione	1.5	0.6
Dehydroepiandrosterone	4.2	1.8
Dehydroepiandrosterone-S	1600	300
Estradiol	0.05	0.013
Estrone	0.08	0.029
Progesterone	0.47	0.17
Testosterone	0.32	0.25

The ovarian failure is compensated by gonadotrophin levels starting to rise, in some women from the age of 30 years. During this time there is evidence for a reduced number of gonadotrophin receptors in perimenopausal ovaries and Inhibin production from granulosa cells falls leading to a reduced Inhibin: FSH ratio. Decompensated failure then occurs due to the critical decline in the oocyte pool leading to further rises in follicle stimulating hormone

(FSH) (10 to 20-fold); Luteinizing hormone (LH) rises only three fold due to its shorter half-life. Oestrogen levels drop due to a reduction in follicle number and qualitative effect on granulosa cell ageing. There is permanent cessation of progesterone production. Studies have shown that the decline in Inhibin B is progressive and not superior to FSH as a predictor of menopause. However, the early follicular phase drop is more readily detectable than FSH as an initial predictor of reduced ovarian reserve and menstrual irregularity (**Edmonds, 2007**).

Other hormonal changes -both adrenal and ovarian androgen levels- start to decline. Some testosterone continues to be produced by ovarian theca cells. Oestrogen therapy can increase sex hormone binding globulin levels which leads to further falls in free androgen levels. The main postmenopausal oestrogen is oestrone which is produced mainly in peripheral adipose tissue and the postmenopausal ovary by aromatization of adrenal androstenedione. The somatotrophic axis becomes less active with ageing leading to insulin resistance and a rise in central adiposity. This in turn leads to the change in body shape from the female gynaecoid shape to the male android shape, itself an independent risk factor for coronary heart

disease. There are a number of factors involved in perimenopausal weight gain including genetic predisposition, socio-economic influences, reduction in caloric need and expenditure, reduced lean body mass and a reduction in resting basal metabolic rate (Edmonds, 2007).

Work is currently being conducted to develop an accurate predictive model for the menopause by combining FSH and Inhibin with anti-Mullerian hormone (AMH) (Edmonds, 2007).

Symptoms:

Immediate consequences:

Immediate consequences of the menopause as hot flushes are thought to arise due to loss of oestrogenic induced opioid activity in the hypothalamus leading to thermo-dysregulation. Other typical immediate menopausal symptoms include insomnia, anxiety, irritability, memory loss, tiredness and poor concentration. Mood disturbances can occur due to fluctuation in hormone levels leading to perimenopausal depression. The menopause transition can also be associated with a significant reduction in sexuality and libido. This is not only because of decreased vaginal

lubrication leading to dyspareunia but also due to the reduction in androgen levels (**Edmonds, 2007**).

Intermediate consequences:

Intermediate consequences of menopause are obvious with oestrogen deficiency leads to the rapid loss of collagen which contributes to the generalized atrophy that occurs after the menopause. In the genital tract this is manifested by dyspareunia and vaginal bleeding from fragile atrophic skin (loss of rugations). In the lower urinary tract, atrophy of the urethral epithelium occurs with decreased sensitivity of urethral smooth muscle and decreased amount of collagen in periurethral collagen. All this results in dysuria, urgency and frequency, commonly termed the urethral syndrome. More generalized changes are seen in the older woman as increased bruising and thin translucent skin which is vulnerable to trauma and infection. A similar loss of collagen from ligaments and joints may cause many of the generalized aches and pains so common in postmenopausal women (**Edmonds, 2007 and Ozdemir, et al., 2009**).

Diagnosis:

With the cessation of follicular activity, major changes in estrogen, progesterone, androgen, and gonadotropin secretion occur within 6 months (**Pernoll, 2001**).

To develop a more functional staging system of reproductive aging, the Stages of Reproductive Aging Workshop (STRAW) was held in 2001. According to the STRAW, reproductive aging is divided into 7 stages (-5 to +2), with -5 beginning with menarche and +2 being defined as the late menopause. This staging system is not applicable to women who smoke, who are at extremes of weight, who engage in heavy aerobic exercise, who have chronic menstrual irregularity, who have undergone hysterectomy, or who have abnormal uterine or ovarian anatomy. (**Decherney et al., 2007**).

The menopausal transition, or perimenopause, is divided into two stages early -2 and late -1 and encompasses a wide age range. Both stages vary in length and both are characterized by an elevation in early follicular phase follicle-stimulating hormone (FSH). In