INTRODUCTION

The chronic Kidney disease –mineral and bone disorder (CKD-MBD) clinical practice guideline by KDIGO suggests that bone mass density testing should not be performed routinely because bone mass density doesn't predict fracture risk as it does in the general population and bone mass density doesn't predict the type of renal osteodystrophy ***(Soichiro et al., 2012).***

As patients with chronic kidney disease may develop renal osteodystrophy, whole body dual energy X -Ray absorptiometry (DEXA) is used to assess bone mineral density ***(Antje et al., 2010).***

Early detection of reduced bone mineral density is an important means of prevention, and dual energy x ray absorptiometry (DEXA) is the most helpful modality ***(El-Husseini et al., 2013).***

DEXA uses the differential attenuation of the tissue through which x ray beam passes to calculate the density of that material ***(Antje et al., 2010).***

Differences in histology among different types of renal osteodystrophy may cause variations in the diagnostic value of DEXA and also in predictive value among the measurement sites because DEXA cannot discriminate bone loss between the trabecula and cortex ***(Soichiro et al., 2012).***

The prevalence of hepatitis c virus among the Egyptian population is one of the highest registered in all age groups ***(Abdel-Aziz et al., 2000; Atkinson et al., 1956).***

AIM OF THE WORK

The aim of this work is to study the effect of hepatitis c virus (HCV) on DEXA scan in prevalent hemodialysis patients.

Chapter (1)

OSTEOPOROSIS AND DEXA

Osteoporosis affects an enormous number of people, of both sexes and all races, and its prevalence will increase as the population ages. Based on data from the National Health and Nutrition Examination Survey III (NHANES III), National Osteoporosis Foundation has estimated that more than 10 million Americans have osteoporosis and an additional 33.6 million have low bone density of the hip ***(National Osteoporosis Foundation, 2002).***

Osteoporosis was first defined in 1940 as a disease of low bone mineral density (BMD). This definition was based on research conducted by Fuller Albright at Massachusetts General Hospital. Dr. Albright took pigeons, removed their ovaries, and noticed that their bones lost density and became weaker. In 1994 the World Health Organization codified this paradigm by creating the official diagnosis of osteoporosis as having low bone mineral density as defined by a "T" score. A T-score is a number of standard deviations from peak bone mass of healthy women aged 20-29. A T-score of -2.5 or less was diagnostic of osteoporosis, while a T-score of -1 to -2.5 is diagnostic of osteopenia ***(Neustadt and Pieczenik, 2012).***

However, the most dangerous aspect of osteoporosis is not a T-score (a number on a test). If you have osteoporosis and fracture a hip, there is a 20% chance of dying within the year.

After a hip fracture only 50% of people regain the same level of independence they had before the injury ***(Gregg et al., 1998).***

And of those who survive the first year, 20% require nursing home care. Thus, a bone density test is only as useful as it can predict whether you will get a fracture. The problem is that since the mid-1990s, research shows that that a bone density test predicts less than half of all people who will fracture. In fact, it only predicts 44% of women and 21% of men who will fracture a bone ***(Cumming et al., 1997).***

Diagnosis of osteoporosis

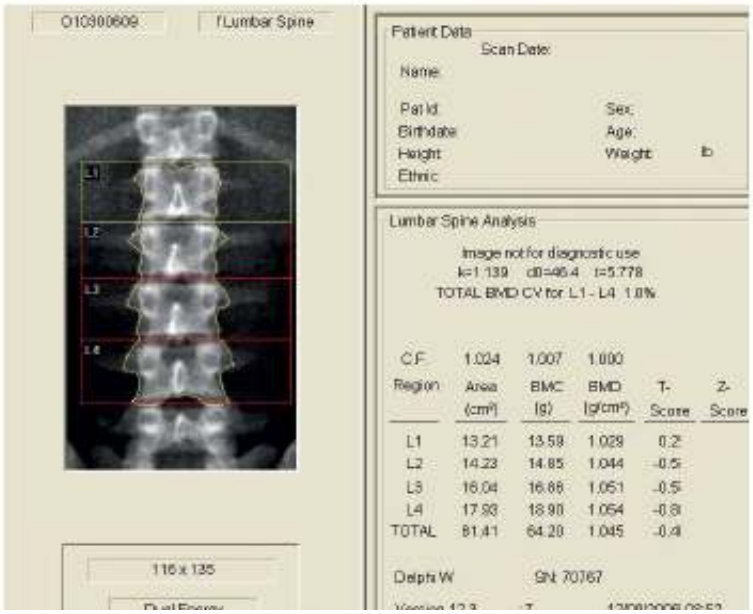

Figure (1): L1 – L4 DXA Scan Report ***(Shepherd et al., 2005).***

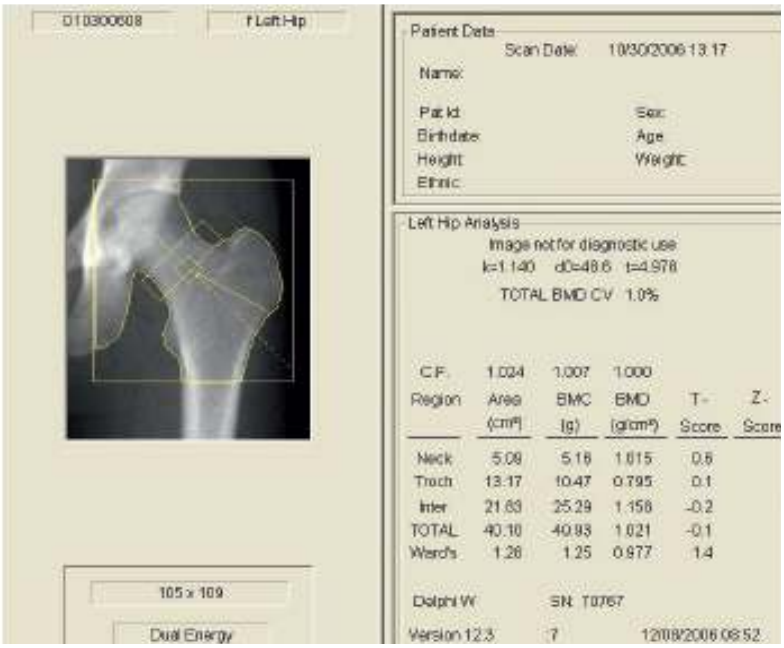

Figure (2): Proximal Femur DXA Scan Report ***(Shepherd et al., 2005).***

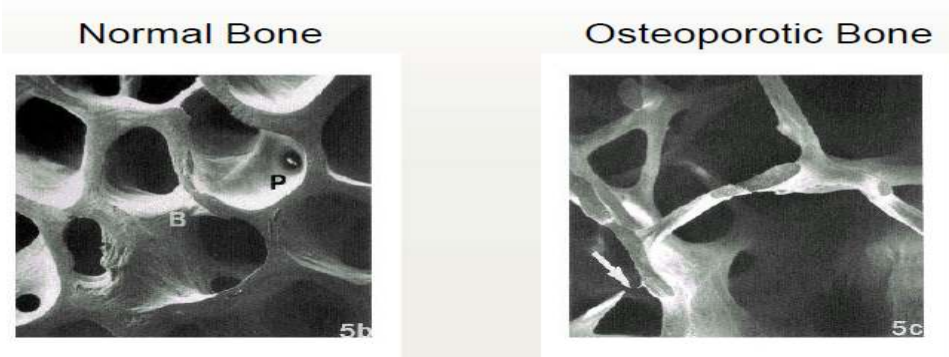

Figure (3): Normal and osteoporotic bone architecture
(Shepherd et al., 2005).

X ray plain films of the hip and spine have been used to assess osteoporosis. The Singh index, a visual assessment of radiopacity of the trabecular tissue in the trochanter, was used to evaluate osteoporosis from plain films of the hip. However, a change of approximately 30% in the trabecular density had to occur before the change could be detected, and X rays needed to be of high spatial resolution, and thus of high dose ***(Kawashima and Unthoff, 1991; Koot et al., 1996).***

The metacarpal index (MCI) is also a technique that can be applied to film X rays. MCI is defined as the ratio of the thickness of the metacarpal cortical shell to the overall diameter. Changes in cortical bone thickness could be quantified with precision, but cortical bone does not turn over and change as quickly as trabecular bone ***(Shepherd et al., 2005).***

When films could be digitalized, techniques such as radiographic absorptiometry (RA) were introduced. Unlike MCI and the Singh index, RA is true absorptiometry; in this case, the quantification of bone density in the phalanges by comparing their X ray absorption to that of different thickness of aluminium ***(Cosman et al., 1991; Yates et al., 1995).***

In the (1970s), DPA and QCT were two of the first absorptiometry methods used for the hip and spine ***(Kraner et al., 1978; Wahner et al., 1983; Richardson et al., 1985).***

DEXA is reliable for evaluating the changes of BMD and bone mineral content at different sites ***(Gal-Moscovici and Sprague, 2007).***

Dual-energy X-ray absorptiometry (**DXA**, previously **DEXA** (**2012)** is a means of measuring bone mineral density (BMD). Two X-ray beams with different energy levels are aimed at the patient's bones. When soft tissue absorption is subtracted out, the BMD can be determined from the absorption of each beam by bone.

Dual energy X- ray absorptiometry (DEXA) is a non – invasive accurate method which estimates bone mineral content and density (BMD) as well as fat and lean body mass. DEXA is widely used in quantitative bone investigation to measure bone mineral density (BMD), (in grams of hydroxyapatite per square centimeter of bone projected area), at the spine and hip level ***(Cochat et al., 1996).***

DXA was introduced commercially in 1987 ***(Stein et al., 1987).***

Although density is typically thought of as a mass per unit volume, DXA can only quantify the bone density as a mass per unit area. The measurement of bone density using a computed tomography (CT) system, called quantitative computed tomography (QCT), can measure the true volume and volumetric bone density. DXA bone density values increase

from birth to adulthood, primarily because the bones become larger. Bone size is also influenced by ethnic differences and sex. Asians typically have lower DXA bone density values compared to sex and age matched Caucasians, partly due to bone size differences ***(Ross et al., 1996).***

DXA defines the composition of the body as three materials having specific X ray attenuation properties: bone mineral, lipid (triglycerides, phospholipid membranes, etc.) and lipid free soft tissue ***(Pietrobelli et al., 1996; Kelly et al., 1998).***

There are relatively few measurements reported from DXA body composition systems, and are available from all DXA scan modes, while the body composition measures are only available from the whole body scan mode ***(Kelly et al., 1989)***:

(1) **BONE MINERAL CONTENT (BMC):** It is the mineral mass component of bone in the form of hydroxyapatite Ca_{10} $(PO_{4)6}(OH)$ $_2$. BMC is typically measured in grams.

(2) **BONE AREA (BA):**BA is the projected area of the bone onto the image plane, typically in cm^2.

(3) **AREAL BONE MINERAL DENSITY (a BMD):** a BMD is the mineral mass of bone per unit image area in g / cm^2.

We measure a BMD = BMC / BA (g / $cm^{2)}$.

The radiation received by the patient during the scan is less than that of an airline flight from California to New York and back ***(Radiologyinfo.org. 2012-04-25).***

There are several DXA regions of interest (ROIs), each of which having unique information to offer. For bone density measurements, regions with higher contents of cancellous (high turnover) bone are more sensitive to osteoporotic and treatment changes. However, longitudinal studies suggest that most ROIs currently defined (spine, femur, radius, and calcaneous) are useful for predicting general fracture risk (i.e. fractures of any bone) ***(Miller et al., 1996).***

DXA used to establish or confirm a diagnosis of osteoporosis, predict future fracture risk and monitor patients by performing serial assessments ***(Kanis, 1994).***

When evaluating bone density using DXA to diagnose osteoporosis, there are several common measurement sites, including the lumbar spine, the proximal hip and the forearm. The standard protocol is to scan two sites, typically the spine and hip. If one of these sites is not available, then the forearm is used. The current standards for using DXA for diagnosing osteoporosis can be found in the position statements of the International Socety for Clinical Densiitometry (ISCD). The most common alternatives to DXA are QCT and quantitative ultrasound (OUS). QCT uses special scan protocols on standard CT systems to quantify volumetric bone densty. QUS is the use

of ultrasound attenuation and the speed of sound to quantify fracture risk and estimate bone density ***(Baims et al., 2008).***

The U.S. Preventive Services Task Force recommends that women over the age of 65 and men over 70 years and older, should get a DEXA

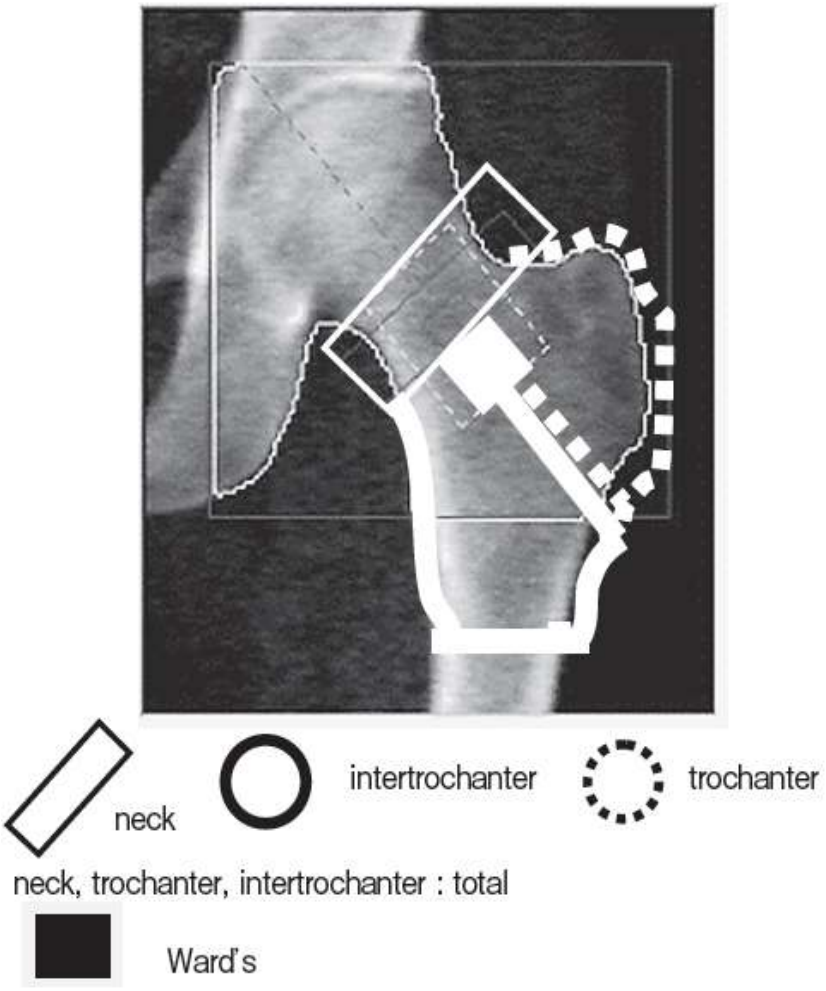

Figure (4): The parts of the proximal femur for BMD measurements ***(Shepherd et al., 2005).***

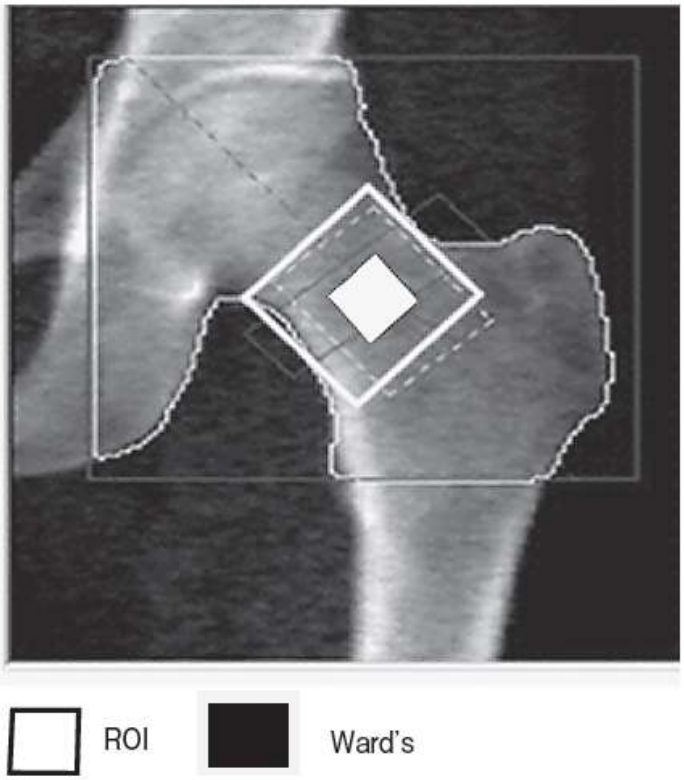

Figure (5): The ward's triangle area determined by Ward's cognitive.

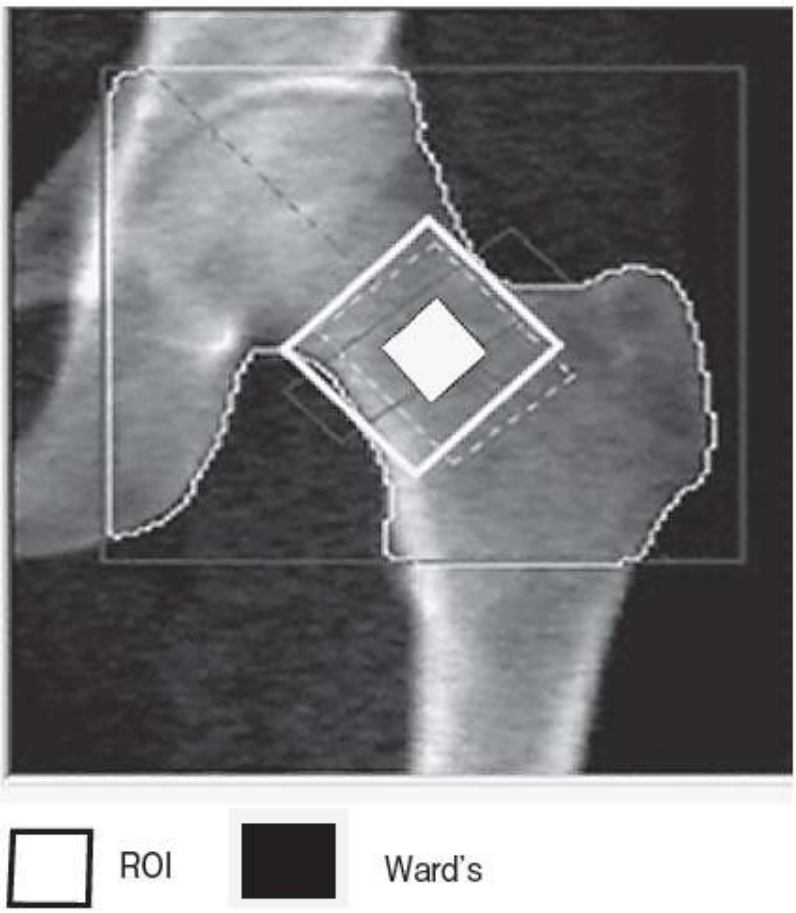

Figure (6): The Ward's triangle area determined by ward's cognitive. ***(Shepherd et al., 2005).***

Bone mass measurements are widely used for diagnosis of osteoporosis, and for identification of patients at risk of fractures ***(Kohno et al., 2009).***

Hip fractures are associated with a 8.4 to 36 percent excess mortality within one year, with a higher mortality in men than in women; additionally, hip fractures are followed by

a 2.5-fold increased risk of future fractures ***(Colón-Emeric et al., 2003).***

A person's risk can be measured using the World Health Organization's FRAX calculator, which includes many different clinical risk factors including prior fragility fracture, use of glucocorticoids, heavy smoking, excess alcohol intake, rheumatoid arthritis, history of parental hip fracture, chronic renal and liver disease, chronic respiratory disease, long-term use of phenobarbital or phenytoin, celiac disease, inflammatory bowel disease, and other risks ***(Screening for Osteoporosis, 2011)*** tested is uncertain ***(Screening for Osteoporosis, 2011).***

Reduced total – hip bone mass has been an independent predictor of all - cause mortality in chronic hemodialysis patients ***(Taal et al., 2003; Kohno et al., 2009).***

In ***(2010), Nickolas et al.*** measured BMD by DEXA and HR-pQCT in 91 pre-dialysis CKD patients. BMD and other parameters measured by the two approaches were associated with fracture history, particularly in patients with a longer duration of and more severe CKD. However neither imaging tool met the investigators' thresholds for "compelling evidence".

Jamal et al. (2012), also set out to determine if BMD by DEXA and HR-pQCT could discriminate fracture status in 211 adult men and women with stages 3 to 5 CKD attending pre-

dialysis clinics in Toronto. While the investigators found that both tests were able to discriminate fracture status, the addition of HR-pQCT measures to BMD by DEXA did not improve fracture discrimination ability. Given the increased cost of HR-pQCT compared to DEXA this suggests its place in BMD screening in CKD will remain limited in the immediate future.

Peak bone mass is determined largely by genetic factors, with contributions from nutrition, endocrine status, physical activity and health during growth.Peak bone mass is achieved in early adulthood, followed by a decline in BMD ***(Khosla and Riggs, 2005).***

Peak bone mineral density (BMD), is a major determinant of osteoporotic fractures later in life, may be lower in Middle East compared with the Western World. Subjects 25 – 35 years of age were randomly selected from greater Beirut. BMD was measured at the lumbar spine, hip, forearm, and total body. Peak BMD in libanese subjects was 0.2 – 0.9 SD below that of peak BMD in American subjects, depending on skeletal site, gender and densitometer ***(Fuleihan et al., 2002).***

An individual's BMD is presented as the standard deviation above or below the mean BMD of the reference population, as outlined in Table 5. The WHO has established the following definitions based on BMD measurement at the spine, hip or forearm by DXA devices: 16 ***(Kanis, 1994).***