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# BONE MARROW PROFILE IN OSTEOPOROSIS


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| **Longjam Nilachandra Singh** | Associate Professor, Department of PMR, RIMS, Imphal |
| **Aten Jongkey** | PG Trainees, Department of PMR, RIMS, Imphal |
| **Longjam Darendrajit Singh** | PG Trainees, Department of PMR, RIMS, Imphal |
| **Shibu B** | PG Trainees, Department of PMR, RIMS, Imphal |
| **Tripti Swami** | PG Trainees, Department of PMR, RIMS, Imphal |
| **Kanti RK** | PG Trainees, Department of PMR, RIMS, Imphal |
| **Akoijam Joy Singh** | Professor, Department of PMR, RIMS, Imphal |


**ABSTRACT** Osteoporosis is a common metabolic bone disease characterized by decreases in bone mass and density. In the adult bone marrow, osteoblasts and adipocytes share a common precursor called mesenchymal stem cells. The plasticity between osteoblasts and adipocytes has important implications in the etiology of bone diseases such as osteoporosis. The pathological conditions linked to osteoporosis can change the bone marrow microenvironment and shift the mesenchymal stem cells fate to favor adipocytes over osteoblasts, and consequently decrease bone mass. A cross-sectional study was conducted in 150 patients (124 females & 26 males) to assess the bone marrow profile in osteoporotic patients, who were diagnosed using Dual Energy X-ray Absorptiometry (DEXA). The study was conducted in the Department of Physical Medicine & Rehabilitation, Regional Institute of Medical Sciences, Imphal, India from February 2015 to March 2016. The study showed that the osteoporotic patients have hypocellular bone marrow.

**KEYWORDS** : osteoporosis, bone mass density, bone marrow, dual energy x-ray absorptiometry, T-Score

## INTRODUCTION

Osteoporosis is a common metabolic bone disease characterized by decreases in bone mass and density and degradation of the bone microstructure, resulting in fragile bones that are prone to fracture. This process is the same for primary and secondary osteoporosis [1]. With an aging population, the incidence of osteoporosis is increasing each year. Osteoporosis causes a higher incidence of fractures, mortality, and morbidity, and is a serious threat to the quality of life of aging individuals [2].

Formation of bone tissue in the embryo and maintenance of bone homeostasis in the adult are largely due to the activity of bone marrow (BM) stem cells called mesenchymal stem cells (MSCs). The dysfunction MSCs may give rise to bone diseases such as osteoporosis [3]. As both osteoblasts and adipocytes originate from MSCs, it is likely that predisposition of bone marrow MSCs to adipocyte lineage at the expense of osteoblasts is a contributing factor to the decreased bone mass. A growing body of evidence has confirmed the reciprocal relationship between these two lineages both in vivo and in vitro [4-6].

A differentiation pathway of BMMSCs involves the progression from osteogenic cells into pre-osteoblasts and finally into osteoblasts. Once the osteoblast has formed, it can secrete several extracellular matrix proteins to control the mineralization of bone matrix. Therefore, the occurrence, proliferation, differentiation, and maturation of osteoblasts are closely related to the normal growth and development of bones, and if any one of these processes is inhibited, a bone growth disorder results. The occurrence of osteoporosis has a direct relationship with an increase in bone resorption and a decrease in bone formation [7].

Physiological BM provides a suitable microenvironment for osteogenesis and the maintenance of bone homeostasis [8]. However, with advanced age, estrogen deficiency, chronic glucocorticoid treatment, and decreased mechanical load, BM microenvironment changes significantly thus providing signals that not only repress osteogenesis, but also favor adipocyte differentiation and formation [9].

World Health Organization (WHO) classify bone mineral density (BMD) using Dual Energy X-ray Absorptiometry (DXA) as normal -1.0 and above, osteopenia -1.0 to -2.5, osteoporosis < -2.5 and severe osteoporosis < -2.5 with fracture.

The objective of this study was to find the bone marrow activity in osteoporotic patients.

## MATERIALS & METHODS

This study was a prospective cross-sectional study done on one hundred and fifty osteoporotic patients presenting to Department of Physical Medicine & Rehabilitation, Regional Institute of Medical Sciences, Imphal between February 2015 & March 2016. Approval from Institutional Ethics Committee and written informed consent was taken from all the patients participating in study.

Bone mineral density (BMD) of the patients was measured using Dual Energy X-Ray Absorptiometry (DXA) scan and T-Score was used for the diagnosis of osteoporosis.

Those patients who were willing to sign the informed consent form, age 45 year and above, and with T-score of < -2.5 were included.

Those patients with T-score -2.5 and more were excluded.

Data analysis was done using Statistical Package for Social Sciences (SPSS) version 21. For descriptive statistics, mean, standard deviation and percentage were used.

## RESULTS & OBSERVATIONS

There were a total of 150 patients included in this study. The mean age of the patients was 67.10 ± 9.50 years. Among 150 patients, 26 (17.3%) were males and 124 (82.7%) were females. The youngest was 45 year and the oldest 95 year old.

The mean T-score of $L_1$ was -2.501± 0.390, $L_2$ was -3.641±0.751, $L_3$ was

-2.658±0.214, $L_4$ was -3.667±0.859, $L_1L_4$ was -2.595±0.008, dual femur neck left -3.522±0.811, dual femur neck right -3.507±0.767, dual femur total left -3.537±0.749 and dual femur total right -3.483±0.670.(Table 1)

**Table 1. Mean T-Score**

| Site | $L_1$ | $L_2$ | $L_3$ | $L_4$ | $L_1L_4$ | Dual femur neck left | Dual femur neck right | Dual femur total left | Dual femur total right |
|---|---|---|---|---|---|---|---|---|---|
| Mean (SD) | -2.991 (0.390) | -3.641 (0.751) | -2.658 (0.214) | -3.667 (0.859) | -2.595 (0.008) | -3.522 (0.811) | -3.507 (0.767) | -3.537 (0.749) | -3.483 (0.670) |

The consistency of bone as denoted by resistance during the bone marrow biopsy were normal in 45 (30%) patients, soft in 102(68%) and hard in 3(2%) only. It was normocellular in 14(9.3%), hypocellular in 105(70%) and hypercellular in 31(20.7%) patients. Predominently micronormoblast in 15(10%), followed by normoblast in 124(82.7%) and megaloblast in 11(7.3%).(Table 2)

**Table 2: Descriptive analysis of bone marrow**

| Consistency N (%) | | Cellularity N (%) | | Erythropoeisis N (%) | |
|---|---|---|---|---|---|
| Normal | 45(30) | Normocellular | 14(9.3) | Predominently Micronormoblast | 15(10) |
| Soft | 102(68) | Hypocellular | 105(70) | Predominently Normoblast | 124(82.7) |
| Hard | 3(20 | Hypercellular | 31(20.7) | Predominently Megaloblast | 11(7.3) |

The leucopoiesis of the bone marrow showed that promyelocyte was low in 49(32.7%), normal in 86(57.3%) and high in 15(10%) of the patients. Myelocyte was normal in 94(62.7%), high in 56(37.3%) and none with low. Metamyelocyte was normal in 86(58.7%), high in 62(41.3%) and the patient with low metamyelocyte was nil. Neutrophil and band forms were low in 4(2.7%), normal in 65(43.3%) and high in 81(54%). Lymphocyte was low in 40(26.7%), normal in 98(65.3%) and high in 12(8%). Blastocyte was low in 125(83.3%) and normal in 25(16.7%) patients. Eosinophil was normal in 126(84%), high in 24(16%) and there was none with low count of eosinophil(Table 3).

**Table 3: Descriptive analysis of leucopoiesis**

| Range | Promyelocyte N (%) | Myelocyte N (%) | Meta-Myelocyte N (%) | Neutrophil N (%) | Lymphocyte N (%) | Blastocyte N (%) | Eosinophil N (%) |
|---|---|---|---|---|---|---|---|
| Low | 49(32.7) | 0 | 0 | 4(2.7) | 40(26.7) | 125(83.3) | 0 |
| Normal | 86(57.3) | 94(62.7) | 86(58.7) | 65(43.3) | 98(65.3) | 25(16.7) | 126(84) |
| High | 15(10) | 56(37.3) | 62(41.3) | 81(54) | 12(8) | 0 | 24(16) |

Megakaryopoiesis was adequate in all 150(100%) patients and myloid:erythroid ratio was within the normal range (normal 2:1-4:1) in all the patients (Table 4).

**Table 4: Megakaryopoiesis and Myloid:Erythroid ratio**

| Megakaryopoiesis N (%) | | Myloid:Erythroid Ratio N (%) | |
|---|---|---|---|
| Reduced | 0 | Normal | 150(100) |
| Adequate | 150 (100) | Erythroid Hyperplasia | 0 |
| Hyperplasia | 0 | Myloid Hyperplasia | 0 |

Plasma cells were normal (0-2%) in 119 (79.3%) and increased in 31 ( 20.7%) patients and there were no abnormal cells like malignant cells for lymphoma etc. and other cells like acid fast bacilli and fungi in none of the patients (Table 5).

**Table 5: Plasma cells, Abnormal cells, Other cells**

| Plasma Cells N (%) | | Abnormal Cells N (%) | | Other Cells N (%) | |
|---|---|---|---|---|---|
| Normal | 119(79.3) | Absent | 150(100) | Absent | 150(100) |
| Increased | 31(20.7) | Present | 0 | Present | 0 |

## DISCUSSION

Osteoporosis is a common metabolic disorder. It commonly affects the elderly, especially post-menopausal women. It is a disease in which both organic and inorganic components of bone are deficient, resulting in a decrease in the total bone mass. The osteoporosis may be symptomless and may be found only by chance. Hence, it may remain largely symptomatic until the occurrence of a catastrophic event, like a fracture of vertebra, hip or other site.

Although osteoporosis is not traditionally considered a disease of vascular origin, recent reports provide indirect evidence of a link between vascular disease and low BMD. For example, Bagger YZ et al [10] in their study on the radiographic measure of aorta calcification found that aorta calcification is an independent predictor of proximal femoral osteoporosis. And Laroche M et al [11] also found that the peripheral vascular disease is independently associated with reduced femoral neck BMD.

Recent studies have expanded the understanding of the function of BM adipose tissue as an endocrine organ capable of secreting different factors to regulate bone metabolism. In a study done by Dong X et al [12] showed that osteoblastic differentiation *in vitro* is inhibited in adipocyte-conditioned media or when co-cultured with adipocytes indicating the negative effect of adipocyte-secreted factors on osteoblastogenesis.

Yeung DK et al [9] in their study on 53 women to evaluate vertebral fat content, and to determine whether bone density correlates with fat content in postmenopausal women found that excessive fat was found in osteoporotic BM.

Wang C et al [13] in their review on the differentiation of bone marrow mesenchymal stem cells concluded that although osteoporosis has a variety of causes, the most basic and direct mechanism is decreased osteogenic differentiation and increased adipogenic differentiation in the bone marrow. With age, the microenvironment in the bone marrow cavity changes, increasing the number of fat cells and inhibiting bone formation. During this process, adipose tissue gradually replaces bone tissue, leading to osteoporosis.

The fat content or adipogenesis is reflected by hypocellularity in the bone marrow. The adipocyte proportion of bone marrow is inversely related to bone formation in osteoporosis.[14]

## CONCLUSION

The study shows predominantly normoblast in 82.7% (124) and hypocellular in 70% (105) of the patients respectively. The leucopoiesis shows promyelocyte in 57.3% (86), myelocyte in 62.7% (94), metamyelocyte in 58.7% (86), lymphocyte in 65.3% (98) and eosinopjil in 84% (126) and all were within normal range, whereas neutrophil was high in 54% (81) and low blastocyte in 83.3% (125). The study also shows adequate megakaryopoiesis and normal myloid:erythroid ratio in all the patients. Plasma cells were within the normal range in 79.3% (119) and increased in 20.7% (31). There were no any abnormal cell like malignant cells for lymphoma etc and other cells like acid fast bacilli and fungi in none of the patients.

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