7. Summary and conclusion

- The mean age of study participants: Group I (Normal bone mass) and Group II (Osteopenia) were 52 years and of group III (Osteoporosis) was higher of 55 years.
- 170 study participants were distributed as: Group I = 57 (33.5%), Group II = 62 (36.5%) and Group III = 51 (30%). 4.1% of group II and 7.6% of group III had sustained fractures.
- In this study population, group I had normal body weight (BMI: 24.9 ± 2), while groups II and III were in pre-obese category (BMI: 26.3 ± 4.2 and 25.5 ± 3.7) respectively. The statistical significant difference observed among the three groups were in waist circumference (p<0.0001), hip circumference (p = 0.002) and waist hip ratio (p = 0.03). This was probably due to high visceral and subcutaneous fat deposition as evidenced by high skin fold thickness in triceps region (p = 0.003).
- Serum calcium was normal in groups I and II (9.5 ± 0.5 mg/dl and 9.0 ± 0.4 mg/dl respectively), while it was in the lower limits of normal (8.4 ± 0.4 mg/dl) in group III. 25 OH vitamin D level was insufficient in groups I and II (25.3 ± 8.3 ng/ml and 21.4 ± 8.1 ng/ml respectively) while it was deficient in group III (19.3 ± 7.2 ng/ml) and with statistical significant difference of p = 0.001.
- hs-CRP levels were increased in groups II and III when compared with group I (p<0.04). The pathogenic damages occurred in the bone was mediated by interaction of inflammatory cells, cytokines, etc.
- High serum total cholesterol and LDLc levels were observed in groups II & III compared to group I.
- Group III had decreased serum sclerostin level of 4.62 ± 1.6 ng/ml compared with group I (5.74±1.3 ng/ml) and group II (4.92±1.4 ng/ml), with statistical significant difference of p<0.0001. It could be due to decreased sclerostin expression caused by apoptosis of osteocytes or deficiency of estrogen or testosterone.
- Serum PINP level was decreased in groups III (178.7 ± 123 pg/ml) and group II (161.2 ± 150 pg/ml) compared with group I (251.5 ± 228 pg/ml). Serum PINP considered as a bone formation marker, was decreased in group III due to less bone formation compared to bone resorption with a significance of p = 0.014.
Serum NTX-I was 219.09 ± 71 ng/ml in group I, 292.1 ± 110 ng/ml in group II and 333.9 ± 322 ng/ml in group III; (p = 0.008). The elevated levels were seen in group III due to increased bone resorption.

Serum CTX-I in group I was 0.81 ± 0.47 ng/ml, in group II 1.07 ± 0.7 ng/ml and in group III 1.14 ± 0.6 ng/ml; (p = 0.02). Serum CTX-I is identified as bone resorption marker.

Group III had mean adiponectin level of 4.6 ± 2.6 µg/mL, group II had 5.2 ± 2.9 µg/mL and group I had 3.96 ± 2.3 µg/mL; (p = 0.044). The increased levels of adiponectin in groups II & III indicated increased adiposity of bone marrow and visceral fat.

Serum FGF 21 levels were 87.02 ± 65.2 pg/mL in group I, 122.2 ± 06.4 pg/mL in group II and 92.3±64.8pg/mL in group III; (p = 0.04). FGF21 is a regulator of bone marrow fat.

In group II, a negative correlation was found between total cholesterol and neck of femur T score (r = -0.242, p = 0.04); also with lumbar spine BMD and T-score (r = -0.332, p = 0.01) and (r = -0.491, p = 0.002) respectively. In group III, a negative correlation was found between triglyceride and neck of femur BMD and T score (r = 0.396, p = 0.004) and (r = -0.386, p = 0.005) respectively; also when compared with lumbar spine BMD (r = -0.288, p = 0.03).

In group II, a negative correlation was observed between serum CTX-I and neck of femur BMD and T Score (r = -0.261, p = 0.04 and r = -0.287, p = 0.02) respectively. The negative correlation between serum NTX-I and lumbar spine BMD and T Score (r = -0.310, p = 0.01 and r = -0.373, p = 0.003) respectively.

In group III, positive correlation was observed between neck of femur T-score and serum sclerostin (r = 0.353, p = 0.01). The negative correlation was observed when neck of femur BMD and neck of femur T-score were compared with serum FGF21 (r = -0.331, p = 0.01) and (r = -0.443, p = 0.001) respectively. Negative correlation was observed between lumbar spine T-score and serum adiponectin (r = -0.349, p = 0.01).

The cut-off level of serum sclerostin (5.6 ng/mL, sensitivity-75%, specificity-70%), serum PINP (171 pg/mL, sensitivity-75%, specificity-70%) and serum CTX-I (0.83
ng/mL, sensitivity-66%, specificity-60%) was derived for the diagnosis of osteoporosis.

- The genotype of LRP5, SNP - rs3736228 (OR = 2.538, 95% CI, p = 0.02) is associated with higher risk of osteoporosis.
- The genotype of COLIA1, SNP - rs180012 (GT allele, OR = 2.036, 95% CI, p = 0.02 and TT allele, OR = 5.892, 95% CI, p = 0.003) was associated with risk of low BMD (groups II & III).
- No association of AdipoQ, SNP - rs266729 gene polymorphism was observed (OR = 1.083, 95% CI, p = 0.424 and OR = 2.528, 95% CI, p = 0.126) between group I and groups II & III together.
- Mean percentage of marrow fat at femur bone in groups II and III was (53.96%). A positive correlation was observed between BMF and serum adiponectin (r = 0.679, p = 0.001), with serum NTX-I (r = 0.445, p = 0.049) and with serum CTX-I (r = 0.332, p = 0.04). A significant negative correlation was found between neck of femur BMD and BMF (r = -0.618, p = 0.004).

- The diagnostic potential of BTMs (serum sclerostin, PINP and CTX-I) in patients with group II & III was fairly high from this study population and serum NTX-I, FGF21 and adiponectin are less potential in predicting osteopenia and osteoporosis.
- Thus these biomarkers provide a better index of bone mass in patients with osteoporosis. Hence these markers play a potential role in the diagnosis of osteoporosis as well as osteopenia.
- LRP5 and COLIA1 SNPs were significantly associated with groups II and III. We have not found significant association of AdipoQ single nucleotide gene polymorphism in our study population.
- There is a strong association between biomarkers (serum adiponectin and serum NTX-I) and bone marrow fat in osteoporotic fractures.
7.1 Limitations of the study

- Since the sample size is small age wise stratification could not be done
- Community based study could give a better picture of rural and urban prevalence of osteoporosis
- Effectiveness of therapeutic interventions could not be done

7.2 Future prospects

- To do a cohort study in both male and female individuals
- To study role of the sclerostin antibody treatment with osteocytic, osteoblastic and osteoclastic cell lineage in osteoporotic and control individuals
- To study the comparison of bone marrow fat between osteoporotic fractures and normal bone fractures by radiological approach
- Study of the possible genetic involvement of other gene polymorphism involved in osteoporosis
- Role of microRNAs in early identification of individuals who are prone for osteoporosis.

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