CHAPTER 5

HOSPITAL BASED SCREENING FOR POST- MENOPAUSAL WOMEN WITH LOW BONE MASS USING LOW COST CONVENTIONAL RADIOGRAPHS

5.1 BACKGROUND

Osteoporotic fractures are an developing problem for healthcare services because, the fact that their frequency is high, and subsequently they are costly to treat [115, 116]. Therefore, effective methods are needed to diagnose those at risk in order to target fracture prevention, treatment [7,117,118] especially in the regard to hip fracture, which is one of the vulnerable osteoporotic fractures with the worst outcome [119, 120]. However, whether their ability to predict hip fracture is better than that of BMD by DXA, or whether they can improve the hip fracture risk assessment of the latter parameter [121]. Also, the combination of bone geometry parameters with BMD-DXA enhances the prediction of hip fracture [12]. While the influence of geometry on fractures has been known for a long time, geometry parameters are not regularly used in fracture risk assessment.

The diagnosis of osteoporosis can be made from radiographs when multiple fractures are present or when the structural abnormalities characteristic of osteoporosis are detected through visual study of reduction in bone density and thinned bone cortices. However, judging BMD by visual observation and interpretation of a radiograph can be imprecise because technical considerations, such as patient size, exposure, and processing factors, influence how dense the bones appear [122].
The cortical bone contributes greatly to bone density measurements, which have been shown to be strongly predictive of future hip fracture risk in our study [14] and others [123]. Cortical thinning is the result of resorption in the cortex. The structural changes seen in cortical bone represent bone resorption at different sites [example, endosteal and intracortical surfaces of the cortex, or within the cortex in the Haversian and Volkmann canals (periosteal)] [124].

The radiologic appearances of osteoporosis are essentially the same no matter and the cause of the problem. Despite the advent of newer and highly accurate and precise quantitative techniques such as DXA and quantitative CT, osteoporosis is still most commonly diagnosed at conventional radiography, in developing countries like India [29].

The mass screening study, who are at risk for low bone mass would be useful were the hip and chest conventional radiographs which are widely available and also cost effective. The accuracy can be improved with conventional radiographs were the prediction of low bone mass is a must in developing countries.

The main objective of this study was to observe the general population of post-menopausal women, who are at risk for low bone mass using low-cost, simple conventional X-ray.

5.2 MATERIALS AND METHODS

5.2.1 Study Design

The method of analysis is as detailed in Figure 5.1
Figure 5.1. Study design
5.2.2 Subjects

A total number of 25 south Indian post-menopausal women, whose age ranged from 46 to 79 years (mean ± SD age = 61.35 ± 9.83 years) were participated in this 3 days hospital-based screening study for low bone mass which was held from 26th to 28th of September 2014 in SRM Hospital, Kattankulathur, Chennai, India. In 25 outpatient women, who have experienced treatment in the orthopaedic division out of which 17 subjects have taken both PA view of chest X-ray and AP view of pelvic X-ray for the diagnosing reason. None of them had chronic illnesses significantly impairing their functional ability, or recognized disorders of calcium metabolism. Based on the inclusion- and exclusion- criteria, all the subjects do not have the previous fracture history were included in this study for further analysis and male subjects have been excluded. Informed consent was obtained from all the subjects, who took part in this study.

5.2.3 Digital X-ray Measurements

5.2.3.1 Digital chest X-ray

A standard digital chest PA view X-ray was taken in all women using a digital X-ray machine (Multiphos, Siemens, Germany). The proper radiographic procedures were followed during acquisition of the image.

From each X-ray, clavicle radiogrammetry measurements were made manually using software (DICOM ruler tool, Scan DOC, Medsynaptic Private, Limited, Pune) and subsequently clavicle bone mass indices were calculated. The brief description of the methodology has been given in Chapter 2, Section 2.2.2.
5.2.3.2 Digital hip X-ray

In each woman a standard pelvic AP view X-ray was taken using a digital X-ray machine (Multiphos, Siemens, Germany). The standard procedures were followed during acquisition of the image. The brief description of the methodology has been given in Chapter 2, Section 2.2.2.

From each X-ray, right femur shaft radiogrammetry measurements were made semi-automatically using FLICM and canny edge detection method using the software tool (MAT LAB, version 2012a). Here the femur shaft was segmented manually, and the geometrical properties were extracted. The brief description of the methodology has been given in Chapter 2, Section 2.2.3. The extracted output feed into the established empirical formula to predict the T.BMD which is detailed in Chapter 4, Section 4.3.4.

5.2.4 Prediction of Total hip BMD

a). Using clavicle radiogrammetry

The prediction T.BMD, was tested by substituting the calculated bone mass indices of clavicle radiogrammetry in the published empirical formula

\[
T.BMD, \text{ g/cm}^2 = [0.47 + 0.003938 (X_1) + 0.420914 (X_2) -5.05139 \times 10^{-4} (X_3)],
\]

where \( X_1 = \% \) CCT of the clavicle, \( X_2 = \) CCT of the clavicle and \( X_3 = \) patient’s age [20].

b). Using proximal femur shaft radiogrammetry

The prediction of T.BMD, was tested by substituting the calculated bone mass indices of femoral shaft radiogrammetry in established empirical formula (Refer Chapter 4, Section 4.3.4. \[
T.BMD, \text{ g/cm}^2 = [0.645- 0.007 (X_1) + 0.013 (X_2) +0.009(X_3)],
\]

where \( X_1 = \) Patient’s age, \( X_2 = \) CCT (mm) of the femoral shaft and \( X_3 = \% \) CCT of the femoral shaft is used to predicting total hip BMD.
5.2.5 Statistical Analysis

Data analysis was done with the SPSS version 17.0 (SPSS Inc., Chicago, USA), Pearson correlation coefficients were obtained for the variables measured in all post-menopausal women studied (n=17). The p value of less than 0.05 (95 % confidence interval) was considered as statistically significant.

5.3 RESULTS

5.3.1 Statistical Correlation

In total women screened (n = 17), the predicted T.BMD by both clavicle-as well as femoral shaft- radiogrammetry measurements were negatively correlated (p < 0.01) with age (r = -0.55 and r = -0.53 respectively). It is also observed that these values decrease with advancing aging as expected. Figures 5.2 and 5.3 shows statistically significant supportive relationship between the predicted T.BMD of using clavicle- and femoral shaft- radiogrammetry with age.

5.3.2 Evaluation of low bone mass

The measured radiogrammetry variables of both clavicle (Fig.5.4) and femoral shaft (Fig.5.5a and b) and the corresponding derived bone mass indices in each screened women are listed in Table 5.1. Also, in each woman, the predicted T.BMD (g/cm^2), using both the published empirical formula involving clavicle radiogrammetry and the established empirical formula involving femoral shaft radiogrammetry are tabulated.

Table 5.2 shows the classification of total women screened using predicted T.BMD by clavicle- and femoral shaft- radiogrammetry. In women, the classification by T-score was carried out using a measured mean value of 1.052 (g/cm^2) and a population SD of 0.152 (g/cm^2) for T.BMD in young normal women aged 25-35 years [69]. According to WHO’s diagnostic criteria, when a threshold of < 0.9 (g/cm^2) was set, it is observed that all women screened
100% (17/17) who were diagnosed having low bone mass when using predicted T-BMD by clavicle radiogrammetry (Fig. 5.6), whereas, 59% (10/17) of total women screened were having low bone mass when using predicted T.BMD by femoral shaft radiogrammetry (Fig. 5.7).

5.3.3 Assessment of future osteoporotic fracture risk

The published [20] osteoporotic fracture threshold values of clavicle radiogrammetry variables of CCT (≤ 4.2 mm) and %CCT (≤ 46.18%) were used in the total women screened. When the threshold value of CCT (mm) alone was used, it is found that 35% (6/17) of post-menopausal women were at future osteoporotic fracture risk; whereas, when the threshold value of %CCT alone was used, it was found that 65% (11/17) of post-menopausal women at future fracture risk. On the other hand, when the threshold values of the combination of both CCT (mm) and %CCT were used, it was found that 35% (6/17) of post-menopausal women were future osteoporotic fracture risk.
Figure 5.2 Statistically significant supportive relationship between the predicted T.BMD using clavicle radiogrammetry and subject’s age (years) in total women screened

Figure 5.3 Statistically significant supportive relationship between the predicted T.BMD using femoral shaft radiogrammetry and subject’s age (years) in total women screened
Table 5.1 Descriptive analysis of the total women screened

<table>
<thead>
<tr>
<th>Post-menopausal women</th>
<th>Age (years)</th>
<th>CLW (mm)</th>
<th>CLw (mm)</th>
<th>CL-CCT (mm)</th>
<th>% CL-CCT</th>
<th>FSW&lt;sub&gt;SA&lt;/sub&gt; (mm)</th>
<th>FSw&lt;sub&gt;SA&lt;/sub&gt; (mm)</th>
<th>FS-CCT&lt;sub&gt;SA&lt;/sub&gt; (mm)</th>
<th>FSCCT&lt;sub&gt;SA&lt;/sub&gt;(%)</th>
<th>Predicted T.BMD (g/cm&lt;sup&gt;2&lt;/sup&gt;) using clavicle radiogrammetry</th>
<th>Predicted T.BMD (g/cm&lt;sup&gt;2&lt;/sup&gt;) using femoral shaft radiogrammetry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>79</td>
<td>11.07</td>
<td>5.64</td>
<td>5.43</td>
<td>49.05</td>
<td>34.43</td>
<td>15.85</td>
<td>18.58</td>
<td>53.96</td>
<td>0.678</td>
<td>0.681</td>
</tr>
<tr>
<td>Case 2</td>
<td>70</td>
<td>10.73</td>
<td>7.40</td>
<td>3.33</td>
<td>31.05</td>
<td>32.35</td>
<td>11.99</td>
<td>20.36</td>
<td>62.94</td>
<td>0.587</td>
<td>0.986</td>
</tr>
<tr>
<td>Case 3</td>
<td>66</td>
<td>11.58</td>
<td>6.38</td>
<td>5.20</td>
<td>44.88</td>
<td>28.71</td>
<td>13.81</td>
<td>14.90</td>
<td>51.90</td>
<td>0.673</td>
<td>0.844</td>
</tr>
<tr>
<td>Case 4</td>
<td>68</td>
<td>10.45</td>
<td>5.76</td>
<td>4.70</td>
<td>44.93</td>
<td>35.57</td>
<td>17.98</td>
<td>17.59</td>
<td>49.45</td>
<td>0.651</td>
<td>0.843</td>
</tr>
<tr>
<td>Case 5</td>
<td>53</td>
<td>11.60</td>
<td>4.33</td>
<td>7.27</td>
<td>62.66</td>
<td>34.52</td>
<td>14.55</td>
<td>19.97</td>
<td>57.85</td>
<td>0.774</td>
<td>1.054</td>
</tr>
<tr>
<td>Case 6</td>
<td>78</td>
<td>12.29</td>
<td>8.73</td>
<td>3.56</td>
<td>28.98</td>
<td>36.90</td>
<td>21.19</td>
<td>15.71</td>
<td>42.57</td>
<td>0.592</td>
<td>0.686</td>
</tr>
<tr>
<td>Case 7</td>
<td>65</td>
<td>11.38</td>
<td>6.41</td>
<td>4.97</td>
<td>43.65</td>
<td>32.90</td>
<td>17.52</td>
<td>15.38</td>
<td>46.75</td>
<td>0.663</td>
<td>0.811</td>
</tr>
<tr>
<td>Case 8</td>
<td>55</td>
<td>10.49</td>
<td>4.55</td>
<td>5.94</td>
<td>56.63</td>
<td>25.27</td>
<td>13.93</td>
<td>11.34</td>
<td>44.88</td>
<td>0.715</td>
<td>0.811</td>
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<tr>
<td>Case 9</td>
<td>60</td>
<td>10.65</td>
<td>5.81</td>
<td>4.84</td>
<td>45.45</td>
<td>30.22</td>
<td>12.62</td>
<td>17.60</td>
<td>58.24</td>
<td>0.661</td>
<td>0.978</td>
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<tr>
<td>Case 10</td>
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<td>11.48</td>
<td>7.71</td>
<td>3.77</td>
<td>32.84</td>
<td>33.67</td>
<td>18.43</td>
<td>15.24</td>
<td>45.26</td>
<td>0.612</td>
<td>0.837</td>
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<td>Case 11</td>
<td>67</td>
<td>11.21</td>
<td>7.82</td>
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<td>30.24</td>
<td>34.12</td>
<td>14.78</td>
<td>19.34</td>
<td>56.68</td>
<td>0.591</td>
<td>0.938</td>
</tr>
<tr>
<td>Case 12</td>
<td>66</td>
<td>10.59</td>
<td>6.93</td>
<td>3.66</td>
<td>34.53</td>
<td>34.04</td>
<td>14.47</td>
<td>19.57</td>
<td>57.49</td>
<td>0.604</td>
<td>0.955</td>
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<tr>
<td>Case 13</td>
<td>46</td>
<td>11.12</td>
<td>7.19</td>
<td>3.93</td>
<td>35.36</td>
<td>32.73</td>
<td>15.56</td>
<td>17.17</td>
<td>52.46</td>
<td>0.626</td>
<td>1.018</td>
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<tr>
<td>Case 14</td>
<td>59</td>
<td>11.99</td>
<td>7.16</td>
<td>4.83</td>
<td>40.30</td>
<td>36.23</td>
<td>20.08</td>
<td>16.15</td>
<td>44.58</td>
<td>0.659</td>
<td>0.843</td>
</tr>
<tr>
<td>Case 15</td>
<td>50</td>
<td>9.23</td>
<td>4.04</td>
<td>5.19</td>
<td>56.21</td>
<td>29.36</td>
<td>16.85</td>
<td>12.51</td>
<td>42.61</td>
<td>0.685</td>
<td>0.841</td>
</tr>
<tr>
<td>Case 16</td>
<td>46</td>
<td>11.71</td>
<td>4.09</td>
<td>7.62</td>
<td>65.10</td>
<td>34.32</td>
<td>14.87</td>
<td>19.45</td>
<td>56.67</td>
<td>0.793</td>
<td>1.086</td>
</tr>
<tr>
<td>Case 17</td>
<td>56</td>
<td>10.46</td>
<td>5.56</td>
<td>4.90</td>
<td>46.87</td>
<td>34.22</td>
<td>19.90</td>
<td>14.32</td>
<td>41.85</td>
<td>0.666</td>
<td>0.816</td>
</tr>
</tbody>
</table>
Table 5.2 Statistical comparison between Predicted T-BMD using clavicle and femoral shaft radiogrammetry in normal and low bone mass post-menopausal women

<table>
<thead>
<tr>
<th>Evaluation of Low bone mass (WHO’s diagnostic criteria)</th>
<th>Normal</th>
<th>Low bone mass</th>
<th>Statistical significance (p &lt; 0.01)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predicted T.BMD (g/cm²) (Clavicle radiogrammetry)</td>
<td>Nil</td>
<td>0.66 ± 0.06</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(n = 17)</td>
<td></td>
</tr>
<tr>
<td>Predicted T.BMD (g/cm²) (Femoral shaft radiogrammetry)</td>
<td>1.00 ± 0.05</td>
<td>0.81 ± 0.05</td>
<td>0.00**</td>
</tr>
<tr>
<td></td>
<td>(n = 7)</td>
<td>(n = 10)</td>
<td></td>
</tr>
</tbody>
</table>

Values represented are pearson’s correlation coefficient (r)

**p < 0.01
Figure 5.4  Manual output of clavicle in sample woman having low bone mass which shows the following measurements $CLW_R = 11.6 \text{ mm}$, $CLW_R = 8.54 \text{ mm}$, $CLW_L = 12.97 \text{ mm}$ and $CLW_L = 8.91 \text{ mm}$, the predicted $T.BMD = 0.592(\text{g/cm}^2)$
Figure 5.5a  Semi-automated output of femoral shaft in sample normal woman: a) Input image with selected ROI, b) Cropped ROI image, c) cluster 1 image, d) cluster 2 image, e) cluster 3 image, f) outer extracted image, g) inner extracted image, h) output image measurements shows $FSW = 30.09$ mm and $Fsw = 12.17$ mm, the predicted $T.BMD = 0.978$ (g/cm$^2$)
Figure 5.5b  Semi-automated output of femoral shaft in sample woman having low bone mass : a) Input image with selected ROI, b) Cropped ROI image, c) cluster 1 image, d) cluster 2 image, e) cluster 3 image, f) outer extracted image, g) inner extracted image, h) output image measurements shows FSW = 35.38 mm and Fsw = 14.77 mm, the predicted T.BMD = 0.819 (g/cm²)
Figure 5.6  Association of Predicted T.BMD (g/cm$^2$) by clavicle radiogrammetry with age in total women screened

Figure 5.7  Association of Predicted T.BMD (g/cm$^2$) of femoral shaft radiogrammetry with age in total women screened
5.4 DISCUSSION

In this mass screening study, it was found that the predicted T.BMD by clavicle and femoral shaft radiogrammetry are negatively correlated with age (p < 0.01). Menopause is the major contributing factor for BMD changes in women as BMD decreases significantly at an average of 8–10% per decade immediately after the menopause [125]. The gradual thinning of femoral cortex with age [86] which shows the CCT decreases in both genders especially in the post-menopausal group. Aging affects the cortical thickness by both endosteal and periosteal widths [110].

Anca et al. advocated with image processing algorithm which detects the lesser trochanter effectively than the manual method and the study derived an empirical formula for predicting the T.BMD, which would be an effective method for the automated process [112]. In this study, the published empirical formula by clavicle radiogrammetry and established empirical formula with the semi-automated process of femoral shaft radiogrammetry will be useful in the evaluation of low bone mass.

Jianhua et al. studied and found that there is a significant increase in accuracy level (p < 0.001), when the manual measurements are compared with semi-automated process in the evaluation [111]. Similarly in this study it was found that there was a high correlation (p < 0.01) with respect to predicted T.BMD of femoral shaft radiogrammetry of normal and low bone mass women using the semi-automated method.

In this study it is found that all post-menopausal women screened were diagnosed as having low bone mass, when using predicted T.BMD by clavicle radiogrammetry, whereas, only 59% of post-menopausal women screened were diagnosed as having low bone mass, when using predicted T.BMD by femoral shaft radiogrammetry.

The mean values of predicted T.BMD using femoral shaft radiogrammetry was lesser significant in post-menopausal women having low bone
mass compared to normal post-menopausal women. A similar study was done by ultrasound technique which shows the post-menopausal women who are at greater risk of low bone mass in developing osteoporotic fractures when compared to normal [125].

When the published fracture threshold values of both CCT (mm) and % CCT of the clavicle was used, it is found that 35% of the post-menopausal women at future osteoporotic fracture risk. The predicted T.BMD using the conventional radiographs can be substituted in the on line FRAX calculator, and thereby one can estimate 10–year probability of both hip and major osteoporotic fracture.

The limitation of the study was given as follows: The T.BMD was not measured by DXA, a ‘gold’ standard for confirmation, but, the earlier study indicated that predicted T.BMD using both clavicle-and femoral shaft-radiogrammetry showed a statistically significant correlation with T.BMD by DXA.

In future using automation in digital X-ray radiogrammetry measurements of both clavicle and femoral shaft in the evaluation of low bone mass can be done with good accuracy and it can be useful as a low-cost screening tool.