ORIGINAL ARTICLE

# Corticosteroid-induced osteoporosis: 10-year fracture risk in Systemic Lupus Erythematosis

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Osteoporosis is of special interest since the last few decades due to its increased fracture risk resulting in increased mortality and morbidity in elderly populations, especially in women. According to the study of Final Part I students supervised by the Preventive and Social Medicine Department using WHO questionnaire forms (Chit-Soe, 2011), prevalence of osteoporotic fracture in Myanmar is 2.4 %. Among 67 rheumatology patients at Rheumatology unit, YGH, prevalence rates were osteopenia (19.3%), osteoporosis (15.8%) for females and osteopenia (20%), osteoporosis (10%) for males (Chit-Soe, 2011). In recent years, as a consequence of the chronic course of the disease and the fact that systemic lupus erythematous affects mostly women and women are more prone to osteoporosis compared to men, osteoporosis has become a major clinical challenge in systemic lupus erythematous as well.

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## Objectives

- To determine the presence of corticosteroid induced osteoporosis in systemic lupus erythematosus patients
- To find the association between demographic, behavioral characters and corticosteroid induced osteoporosis in systemic lupus erythematosus (SLE) patients
- To determine the 10 year fracture risk in current steroid user less than three months or non- user in SLE patients
- To determine the 10 year fracture risk in current steroid user more than three months in SLE patients.
- To compare the 10 year fracture risk between current steroid user less than three months or non- user and current steroid user more than three months in SLE patients

## Materials and methods

It was a hospital based cross-sectional analytic study carried out in Rheumatology clinic at Outpatient Department and Medical wards of Yangon General Hospital and New Yangon General Hospital. Study period was for 12 months (From January 2012 to December 2012). Inclusion criteria of the patients were age above 12 years, current steroid users more than three months or non-users and current steroid users less than three months. Exclusion criteria were patients with other diseases associated with osteoporosis such as rheumatoid Arthritis, thyrotoxicosis, Cushing's disease and postmenopausal patients .

All eligible patients were recruited; 98 patients with SLE were interviewed and enrolled for the study. Of them, only 68 patients were followed-up with bone mineral density measurements and the rest dropped out. Data from 68 SLE patients were recorded and statistically interpreted. Informed consent was taken before interviewing using structured questionnaires. The following clinical data were collected by interview with patients: Demographic variables: age, sex, height, weight, menstrual history, smoking, alcohol, disease duration, drug history including corticosteroids and immunosuppressive drugs. Bone Mineral Density of the calcaneus was measured with *OsteoPro*, Quantitative ultrasound. WHO Fracture risk assessment tool was then used to estimate the 10-year fracture risk. All data were recorded in data sheet and data analysis was done. The collected data were entered into Microsoft excel and analysed with SPSS 11.5.

## RESULTS

The age of the respondents ranged from 15 to 48 years with a mean age of 29.94± 8.39. The most common age group was 30-39 years which represented 36.8% of the study population. The weight of the respondents ranged from 29 to 84.40 kg with mean weight of 48.4453± 1.03504. The height of the respondents ranged from 140 to 167 cm with mean height of 1.554± 6.81279. The BMI of the respondents ranged from 13.2 to 31.8 with mean BMI of 19.9691± 3.84321. BMI was generally normal or underweight each of which represented 44.1% of study population. Of all the study population, there were only 2 who had history of previous fracture and parental hip fracture. None of the SLE patients in the study smoked nor drank alcohol. The cumulative steroid dose of the respondents ranged from 0 to 243.27 mg with the mean cumulative steroid dose of 20.64± 35.7. The total steroid dose of the respondents ranged from 0 to 17615 mg with the mean of 2970.8± 3600.4 mg. The total duration of steroid therapy of the respondents ranged from 0 to 1361 days with the mean duration of 220.05± 296.84.

The BMD of the respondents ranged from -3.62 to -0.04 with the mean BMD of -1.6562± -0.74441. The most common was osteopenia which represented 69.1% of study population.

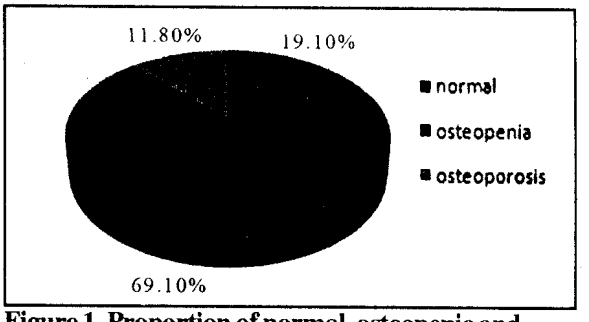


**Figure 1. Proportion of normal, osteopenic and osteoporosis patients**

The 10 year risk for hip fracture of the respondents ranged from 0 to 5.4 with the mean risk of 0.475± -0.79125. The 10 year risk for major

osteoporotic fracture of the respondents ranged from 0 to 6.8 with the mean risk of 1.6059± 1.07271. In the present study, only 19.1 percent of the study population had normal bone mineral density, while about 70 percent had osteopenia and 11.8 percent had osteoporosis. Impaired bone mineral density was seen in about 80 % of the SLE patients. However, there is no statistically significant association between age groups and bone mineral density. (Pearson's chi-square= 1.073, P=0.297)

Moreover, no association between gender and bone mineral density was found as there was more prevalence of SLE in females than males. Most of the SLE patients are normal or underweight (approximately 88 %) and these SLE patients had impaired bone density. However, there was no significant association between BMI and bone mineral density among SLE patients (Pearson's chi square= 1.981, p=0.162). There was no association found between the duration of steroid therapy (less than 3 months vs more than 3 months) and the bone mineral density (Chi= 0.002 p=0.964).

The fracture risk assessments in two groups of steroid users are calculated by FRAX tool. The mean of hip fracture risk in steroid non-user is 0.3452±0.5436, t is -1.244 and among user is 0.5838±0.9535. Statistically there is no significance difference between risk of hip fracture among steroid non-users and users (p value is 0.218). In contrast, the 10 year risk for major osteoporotic fracture among steroid non-user is 1.3065±0.9007 and among non-user is 1.8568±1.1504.

There was a statistically significant difference in major osteoporotic fracture risk between steroid user and non-user (p= 0.034). In addition, we studied the total steroid dose, cumulative steroid dose and duration of steroid therapy and their effect on bone mineral density. There was no relation between total steroid dose, cumulative steroid dose and duration of steroid therapy and impaired bone mineral density.

## DISCUSSION

This study has been unable to provide evidence that bone mineral density is correlated with age, sex, BMI, and other risk factors such as previous fracture, history of parental fracture hip, smoking, alcohol drinking, duration of steroid (whether less than three months or more than three months or total duration), cumulative steroid dose and total steroid dose. A similar finding was observed in one study. Dhillon et al (1990) showed that no correlation was found between BMD and the following variables: height, weight, and body mass index, age, smoking, and alcohol intake,duration of steroid treatment and dose of steroid.

The findings did not seem to be consistent with other research results. In a study of the osteoporotic effect of long term corticosteroid therapy in chronic steroid users in NOGH and YGH by Soe-Yu-Zaw (2011) it was found that bone density had statistically significant association with age ($P < 0.001$), sex (females had statistically significant decreased bone density than males in the present study ($P < 0.05$)). However, similar to the present study, there was no statistically significant association between body mass index ($P > 0.05$), previous low-energy trauma fracture ($P > 0.05$), smoking ($P > 0.05$), alcohol drinking status and bone density. In contrast to the present study, low bone density was found to have a statistically significant association with increased duration of steroid therapy ($P < 0.05$).

Our finding also did not support the findings from the previous research by Cho-Cho. In Cho-Cho (2006) study, the odds ratio showed that advancing age was highly correlated with osteoporosis. Women in the two older age groups

(60-69 years and ≥ 70 years) had a significantly greater likelihood (OR 1.99 95% CI 1.06, 3.75) of osteoporosis than those in the youngest age group (50-59 years) (OR 4.85 95% CI 2.86, 8.21). In Cho-Cho's study, women in the highest quintile of weight (≥ 75Kg) were at an approximately fivefold reduced risk of being in the lowest tertile compared with those in the lowest quintile of weight (OR for women ≥ 75 kg compared with those < 75 kg = 0.2, 95% CI 0.1, 0.3). Similarity with the present study was that women with BMI ≤ 25 Kg/m$^2$ had 2.05 times risk for osteopoenia and osteoporosis than women with BMI > than 25 Kg/m$^2$ (OR = 2.05) although statistically not significant (P=0.092).Also, there was no statistical difference in risk of clinical discordance of bone density with smoking (1.000).

In the present study, only 19.1 percent had normal bone mineral density and 69.1 % had osteopenia, 11.8 % had osteoporosis regardless of steroid therapy status. The study obtained similar findings as those found in other studies showing the high prevalence of osteoporosis and reduced BMD in SLE. M. Boyanov et al (2003) found that 68.7 % had osteoporosis at one major site at least (AP or lateral spine, total hip and total forearm). Only 12.5 % had normal bone density values at all sites. 18.8% of the controls had osteoporosis at one major site at least, 37.5% had osteopenia and 47.7% had normal BMD.

However, this study was unable to correlate between steroid therapy and bone loss. A possible explanation for this result might be due to the fact that SLE disease itself had notorious effect on bone metabolism so that there was high prevalence of impaired bone density regardless of the therapy they received.

The 10 year fracture risk assessment by FRAX tool in steroid non-user and steroid user showed that there was no significant difference between hip fracture risk and steroid treatment. On the contrary, there was risk of increased major osteoporotic fracture risk in steroid user than in steroid non-user. It was statistically significant. These findings are consistent with those in Rhew EY et al(2008) study saying that higher prevalence of vertebral fractures had been found in female SLE patients than in age-matched controls.

Formiga et al (1995) had shown a high percentage of patients with low BMD in a population of 74 SLE young, premenopausal subjects: nine of our patients (12 1%) had BMD below the reference range indicating osteoporosis. It was found that the bone mass of the lumbar spine and femoral neck to be less in this group of SLE patients than in control subjects (p < 000 1). Fractures were not found. The patients in their study had a high mean cumulative dose of prednisone and a high mean dose of prednisone at the time of the study, but there was no relation between dose of glucocorticoid therapy and BMD in the lumbar spine or femoral neck.

The results confirm those of Dhillon et al in premenopausal SLE patients, which also showed no correlation between cumulative dose of prednisone and BMD, and no fractures. However, Dhillon et al., found a lower frequency of osteoporosis, reporting a low BMD in one (4.5%) of 22 SLE patients-admittedly a small sample size. EK Li et al (1998) study also showed that BMDs in SLE patients were significantly lower at the lumbar spine (p=0.001). However, multiple stepwise regression analysis in the SLE patients revealed no correlation between BMD and corticosteroid (average daily dose, cumulative dose or duration of treatment), age, height, weight, alcohol intake, cigarette smoking though BMI was consistently correlated with BMD at all sites (r=0.35-0.67).

The present study showed that the results were opposite to the previous study by Chit-Soe

et al (2011) which showed that rheumatology patients who were taking steroid for more than 3 months had a significant association with osteoporosis.

## CONCLUSION

This study highlights the high prevalence of osteoporosis and reduced BMD in SLE patients. It is therefore important to use bone protecting measures including screening procedures to detect early bone loss, lifestyle changes and medical therapy where needed to help those SLE patients who are expecting longer life expectancy due to advanced therapy as well as steroid therapy. There is also a need to have awareness of the risk of osteoporotic fracture in long term steroid treated SLE patients. We need to pay more attention to prevent these fractures.

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