

ORIGINAL ARTICLE

Risk Factors for Osteoporotic Fracture: A Case Control Study

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Abstract

Introduction: Osteoporosis is a global problem and affects every geographical area. Estimates indicate that as many as 50% of Americans older than 50 years will be at risk for osteoporotic fractures during their lifetimes. Hip fracture is also a major public health problem in Asia. It has been projected that by the next century, 50% of all hip fractures in the world will occur in Asia. Rates for women are higher than those for men and rates for all demographic groups increase with age. Older persons have much higher fracture rates than younger persons with the same bone density because of increasing risks from other factors, such as bone quality and tendency to fall. All types of fractures are associated with higher mortality rates. Men are more likely than women to die in the year after a hip fracture, with mortality rates for men estimated at up to 37.5%. This study was done with the aim to find out the risk factors for osteoporotic fracture in Bangladeshi population as there is no such previous studies in Bangladesh.

Methods: A case control investigation was done comprising 181 cases admitted with osteoporotic fracture into two tertiary hospitals in Dhaka with 1:1 ratio of age and sex matched controls from July 2017 to June 2019. Information from all subjects was obtained through a questionnaire-based interview.

Results: There was a significant increase in the number of cases of osteoporotic fracture with increasing age comprising 88.5% in 61–80-year age group. There were significantly more women (60.7%) than men (39.3%). Univariate analysis identified use of steroid, thyroid medication, loop diuretics, history of previous fracture, kidney disease, arthritis, immobilization, family history of osteoporosis, loss of height and lack of consumption of adequate dairy products (<3 servings/day) as the risk factors of osteoporotic fracture. As expected in multivariate modeling, numerous risk factors had a reduced effect after adjustment for potentially correlated covariates. The statistically significant factors were – use of steroid (OR 3.19, CI 1.10 – 9.22), loop diuretics (OR 5.00; CI 1.29 – 19.46), arthritis (OR 3.49; CI 1.49 – 8.18), family history of osteoporosis (OR 5.45; CI 1.29 – 23.13) and loss of height (OR 2.96; CI 1.27 – 6.88).

Conclusions: This study has demonstrated some risk factors associated with osteoporotic fracture such as use of steroid and loop diuretics, arthritis, family history of osteoporosis and loss of height. But some known risk factors for osteoporotic fracture, e.g. lack of physical exercise, immobility, inadequate intake of diet rich in calcium content, caffeine, smoking, immature menopause, etc. were not found statistically significant in this study may be due to small study sample, selection bias or recall bias.

Keywords: Osteoporosis, Fragility fracture, Bone mineral density

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Introduction:

Osteoporosis is a systemic skeletal condition characterized by low bone mass and micro architectural deterioration of bone tissue that increases bone fragility and risk for fractures.¹ Osteoporosis is diagnosed in persons on the basis of presence of a fragility fracture or by bone mass measurement criteria. Osteoporosis is diagnosed when the bone mineral density (BMD) at the spine, hip or wrist is 2.5 or more standard deviations (SDs) below the reference mean (T-score of -2.5 or less), and low bone density or mass is diagnosed when BMD is from 1.0 to 2.5 SDs below the reference mean.²

Osteoporosis is a global problem and affects every geographical area. Estimates indicate that as many as 50% of Americans older than 50 years will be at risk for osteoporotic fractures during their lifetimes.¹ It has been projected that by the next century, 50% of all hip fractures in the world will occur in Asia.² Rates for women are higher than those for men; rates vary by race, with the highest rates in white persons; and rates for all demographic groups increase with age.³⁻⁶ Older persons have much higher fracture rates than younger persons with the same bone density because of increasing risks from other factors, such as bone quality and tendency to fall.⁷ All types of fractures are associated with higher mortality rates.⁸⁻¹¹ Men are more likely than women to die in the year after a hip fracture, with mortality rates for men estimated at up to 37.5%.¹² Osteoporosis may occur due to specific disorders (hyperthyroidism, hyperparathyroidism, prolonged immobilization, chronic liver disease) or drug. There are several other risk factors for osteoporosis like thin built, sedentary lifestyles, diet low in calcium and vitamin D, excess alcohol consumption, cigarette smoking/tobacco use, premature or surgical menopause, etc. Others include a family history of osteoporosis or atraumatic fractures.¹³

In our country osteoporotic fracture is not uncommon but there is no published data about the risk factors. The aim of this study was to determine the risk factors of osteoporotic fracture in the Bangladeshi population, as a first step in preparing public health measures and to enable later monitoring and evaluation of the governmental strategy.

Methods:

This case-control study was carried out in National Institute of Traumatology and Orthopaedic Rehabilitation (NITOR) & Shaheed Suhrawardy Medical College Hospital (ShSMCH) for a period of 2 years from 1st July, 2017 to 30th June, 2019. Admitted cases of confirmed osteoporotic fracture was selected for the study. Those who had other types of fracture admitted in the hospital or healthy attendants of the patients were controls. As there was no

known prevalence in our country, measuring the power of the study at 20% with significance level set at 0.05, the sample size was calculated 181 for each case and control group. The sampling technique was convenience sampling and this sampling technique was used as per inclusion and exclusion criteria. Difficulty getting up from a chair was used as proxy for testing agility on both cases and controls. If the subject gave a history of not being able to get up from a chair effortlessly or without external assistance (prior to sustaining hip fracture), he or she was classified as positive.¹⁴ All the patients aging e" 50 years who had osteoporotic fracture in neck of femur, spine or Colles' fracture within the last 3 months were included and debilitated, non-cooperative, patients with dementia or psychiatric illness and patients not willing to enter into the study were excluded from the study. Ethical clearances were obtained both from NITOR and ShSMCH ethical review committees and informed written consents from the patient and control were secured. Data collection form was filled by interrogating the patient or care giver. All data were recorded systematically in preformed data collection form (questionnaire) and quantitative data were expressed as mean and standard deviation and qualitative data were expressed as frequency distribution and percentage. During analysis Chi-square test was done for the comparison of qualitative variables and student t test was used for the comparison of continuous variables. Multivariable linear regression was used to assess the significance of covariate-adjusted relations between the continuous variables. Multivariate logistic regression was performed to measure the odds ratio (OR) among qualitative variables. Regression models were crude, age and sex adjusted and fully adjusted. Statistical analysis was performed by using windows based computer software devised with Statistical Packages for Social Sciences (SPSS-20) (SPSS Inc, Chicago, IL, USA). A p value of 0.05 (two-tailed) or a 95% confidence interval (CI) not including the null point was regarded as statistically significant.

Results:

General characteristics of both case and control subjects are shown in Table I. There were no significant differences between the case patients and control subjects with regard to age. More cases than controls appeared to be on long term medication for chronic illnesses. The distribution of osteoporotic fractures between the sexes was interesting as 60.7% of the fractures occurred in females and only 39.3% in males. Age between 61-80 years appeared to be a major risk group with 88.5% of the osteoporotic fractures studied occurring in this age group.

Table I
Characteristics of Cases and Controls

Variables		Case (%)	Control (%)
Note: Plus - minus values are Means $\pm$ Standard Deviations		(N=181)	(N=181)
Sex Distribution	Male	71 (39.3)	71 (39.3)
	Female	110 (60.7)	110 (60.7)
Mean Age		67.9 $\pm$ 5.8	65.0 $\pm$ 5.1
	Male	68.6 $\pm$ 5.7	65.0 $\pm$ 5.7
	Female	67.4 $\pm$ 5.9	65.0 $\pm$ 4.8
Marital Status	Married	157 (86.9)	153 (84.4)
	Others	24 (13.1)	28 (15.6)
Occupation	Housewife	98 (54.1)	95 (52.5)
	Business	39 (21.6)	27 (14.9)
	Service	15 (8.3)	27 (14.9)
	Others	29 (16.0)	32 (17.7)
Socio-Economic Status	Upper	12 (6.6)	15 (8.3)
	Middle	30 (16.6)	39 (21.5)
	Lower	139 (76.8)	127 (70.2)

Univariate Analysis

The OR and 95% CI estimated by univariate logistic regression modelling for variables identified by previous research as possible risk factors for osteoporotic fractures in other populations are presented in Table II.

Diet and lifestyle

Assessing the risk factors regarding dietary habit and lifestyle, the factors looked for were diet containing high protein, vegetarian diet, dairy products, consumption of caffeinated beverages (tea or coffee) and alcohol and above all exercise habit.

Table II
Distribution and Analysis of Selected Variables in Cases and Controls

Variables	Case (%) n = 181	Control (%) n = 181	Odds Ratio (95% CI)	P-value
Steroid	56 (31.0)	21 (11.6)	3.49 (1.34 – 9.08)	0.008
Thyroid medication	24 (13.3)	3 (1.7)	9.06 (1.10 – 74.81)	0.015
Loop diuretics	39 (21.5)	12 (6.6)	3.86 (1.18 – 12.62)	0.019
Previous fracture	51 (28.2)	12 (6.6)	5.51 (1.73 – 17.53)	0.002
Liver disease	21 (11.6)	6 (3.3)	3.82 (0.76 – 19.21)	0.163
Kidney disease	39 (21.5)	12 (6.6)	3.86 (1.18 – 12.62)	0.034
Diabetes mellitus	53 (29.3)	36 (19.9)	1.71 (0.74 – 3.95)	0.207
Gastrectomy	12 (6.6)	3 (1.7)	4.21 (0.46 – 38.81)	0.365
Arthritis	101 (55.8)	51 (28.2)	3.26 (1.53 – 6.93)	0.002
Immobilization	30 (16.6)	6 (3.3)	5.78 (1.21 – 27.63)	0.030
Family h/o osteoporosis	42 (23.2)	9 (5.0)	5.76 (1.56 – 21.24)	0.007
Loss of height	101 (55.8)	59 (32.6)	2.58 (1.23 – 5.39)	0.011
Smoking	59 (32.6)	47 (26.0)	1.37 (0.63 – 3.00)	0.427
Lack of high protein diet	134 (74.0)	131 (72.4)	1.09 (0.49 – 2.42)	0.839
Vegetarian	15 (8.3)	6 (3.3)	2.63 (0.49 – 14.13)	0.439
Dairy product consumption(<3 meals/week)	145 (80.1)	116 (64.1)	2.30 (1.02 – 5.23)	0.043
Tea/Coffee drinking(>3 cups/day)	71 (39.2)	68 (38.0)	1.07 (0.52 – 2.22)	0.852
Inadequate exercise(<3 times/week)	83 (45.6)	68 (37.6)	1.40 (0.68 – 2.89)	0.359

Among these factors, only inadequate dairy product consumption (<3 meals/week) was found to be statistically significant (OR 2.30; 95% CI 1.02 – 5.23; $p = 0.043$). None of the subjects in case and control gave any history of alcohol consumption. Though vegetarian diet had an OR of 2.63, the 95% CI was ambiguous (0.49 – 14.13). Similarly smoking, tea/coffee drinking and inadequate exercise (<3 times/week) did not give any statistically significant result.

Illnesses and medications

To assess the risk factors regarding illnesses and medications, several chronic illness, e.g. liver disease, thyroid disorder, kidney disease, epilepsy, diabetes mellitus, gastrectomy, rheumatoid (or other) arthritis, prolonged immobilization, Paget's disease, etc. and long term medication history, e.g. steroid (prednisone, cortisone etc.), thyroid medication, anticonvulsants, loop diuretics, heparin, chemotherapy, etc. were obtained. Among the risk factors, several factors were found statistically significant.

They were steroid (OR 3.49; CI 1.34 – 9.08; $p = 0.008$), thyroid medication (OR 9.06; CI 1.10 – 74.81; $p = 0.015$), loop diuretics (OR 3.86; CI 1.18 – 12.62; $p = 0.019$), history of previous fracture (OR 5.51; CI 1.73 – 17.53; $p = 0.002$), kidney disease (OR 3.86; CI 1.18 – 12.62; $p = 0.034$), rheumatoid (or other) arthritis (OR 3.26; CI 1.53 – 6.93; $p = 0.002$), immobilization (OR 5.78; CI 1.21 – 27.63; $p = 0.030$). None from the study population gave history of using

heparin, anticonvulsant or any chemotherapeutic agent. Liver disease, diabetes mellitus and history of gastrectomy gave statistically non-significant results.

Others

Among other risk factors, family history of osteoporosis and loss of height were found to be statistically significant risk factor [(OR 5.76; CI 1.56 – 21.24; $p = 0.007$) and (OR 2.58; CI 1.23 – 5.39; $p = 0.011$) respectively]. Some risk factors only for the female participants, e.g. immature menopause, hysterectomy, oophorectomy, etc. were assessed none of which were statistically significant. (Table III)

Multivariate Analysis

Table IV presents the adjusted odds ratios, 95% confidence intervals, and p values of a multivariate logistic-regression model determined by stepwise selection. As expected in multivariate modelling, numerous risk factors had a reduced effect after adjustment for potentially correlated covariates. The factors that were statistically significantly associated with osteoporotic fracture were – use of steroid (adjusted OR 3.187; CI 1.102 – 9.220; $p = 0.032$), loop diuretics (adjusted OR 5.002; CI 1.286 – 19.459; $p = 0.020$), rheumatoid (or other) arthritis (adjusted OR 3.492; CI 1.491 – 8.177; $p = 0.004$), family history of osteoporosis (adjusted OR 5.452; CI 1.285 – 23.134; $p = 0.021$) and loss of height (adjusted OR 2.961; CI 1.274 – 6.882; $p = 0.012$).

Table III
Distribution and Analysis of Selected Variables in Cases and Controls (Females only)

Variables	Case (%) n = 110	Control (%) n = 110	Odds Ratio (95% CI)	P-value
Immature menopause	21 (19.1)	6 (5.5)	4.08 (0.79 – 21.16)	0.075
Hysterectomy	12 (10.9)	9 (8.2)	1.37 (0.29 – 6.61)	1.000
Oophorectomy	12 (10.9)	9 (8.2)	1.37 (0.29 – 6.61)	1.000
Uterine malignancy	12 (10.9)	9 (8.2)	1.37 (0.29 – 6.61)	1.000

Table IV
Multivariate Analysis of Risk Factors for Osteoporotic Fractures

Variables	Adjusted Odds Ratio (95% CI)	p - value
Steroid	3.187 (1.102 – 9.220)	0.032
Loop diuretics	5.002 (1.286 – 19.459)	0.020
Arthritis	3.492 (1.491 – 8.177)	0.004
Family h/o osteoporosis	5.452 (1.285 – 23.134)	0.021
Loss of height	2.961 (1.274 – 6.882)	0.012

Discussion:

Osteoporotic fracture is increasingly becoming a major health problem in Bangladesh and knowledge about risk factors is essential for its prevention. Although many large scale studies have been reported in White and Asian (other than Bangladeshi) populations, there is currently no research available on variables that increase the risk of osteoporotic fracture in the Bangladeshi population. This case control study revealed many vital risk factors for an urban Bangladeshi population.

Risk factors were assessed by interview through a standardized questionnaire. This analysis focused on identifying risk factors for osteoporotic fracture in the univariate and multivariate setting. A number of risk factors that were significant in the univariate analysis were not included in the final model produced by the stepwise selection routine. This is anticipated as the correlation between the risk factors may reduce their relative importance. In addition, effect modification may be present amongst the risk factors based on a comparison of odds ratios yielded by the univariate and multivariate models. For example, the effect loop diuretics is significantly elevated in the multivariate model. This suggests that the effect of loop diuretics is modified by the presence of another risk factor in the multivariate model. Future investigations may include an in-depth analysis of interactions.

In this study, in univariate analysis, it was found that use of steroid, thyroid medication, loop diuretics, history of previous fracture, kidney disease, rheumatoid (and other) arthritis, immobilization, family history of osteoporosis, loss of height and lack of dairy product consumption were associated with risk of osteoporotic fracture. Whereas in multivariate analysis, only risk factors found to be significant were use of steroids, loop diuretics, rheumatoid (and other) arthritis, family history of osteoporosis and loss of height.

In the Mediterranean osteoporosis study conducted in Europe, it was found that late menarche, poor mental function, low BMI, lack of physical activity, low exposure to sunlight, and low consumption of calcium and tea to be significantly associated with the risk of hip fracture.¹⁵ In the Asian osteoporosis study, low dietary calcium intake, lack of physical activity, alcoholism and cigarette smoking found to be risk factors for hip fracture.¹⁶ Similarly, in Japan, one study found a low BMI, regular alcohol intake, prevalent vertebral fracture, having 5 or more children, a low milk intake and later age at menarche to be associated with risk of hip fracture.¹⁴ Unlike the American and

European population where the prevalence of osteoporotic fractures in women is more than twice than that of men in any age group,¹⁷ the ratio in the Bangladeshi population appears to be 60.7% to 39.3%. Future research could explore this discrepancy. One possible reason could be the disparity in life expectancies in the different populations. In the year 2019, life expectancy at birth was 70.71 years for Bangladeshi males and 75.09 years for Bangladeshi females.¹⁸ However the life expectancy at birth was 75.2 years for American males and 80.4 years for American females.¹⁹ In this study, the BMI could not be assessed as most of the cases were bed-ridden and they did not have previous data regarding measurements of weight or height to calculate the BMI which is a strong risk factor for osteoporotic fracture. According to the previous research,²⁰⁻²³ men and women with a lower BMI are at a significantly higher risk for osteoporotic fracture than their heavier counterparts. It has been suggested by these prior studies that this protection is a result of increased adipose tissue-based production of estrogen, more padding around the hips that may decrease the energy transmission from the impact of the fall to the proximal femur, and the greater gravitational forces on bone mass.^{22,24} However, this study did not examine the body distribution of adipose tissue as well. In contrast with previous research, lack of physical activity was not found to be a risk factor for osteoporotic fracture.^{16,22,25} As a major portion of both cases (45.6%) and controls (37.6%) acknowledged that they were not accustomed to any kind of physical exercise even as less as three times per week which may be an effect of rapid urbanization of the country and lack of knowledge of importance of physical exercise. Dietary calcium was assessed qualitatively in this study by food frequency questionnaire. If the participant consumed less than 3 dairy products a day (1 serving = 8 oz. milk, 1 oz. cheese, container of yogurt or serving of ice cream), he/she was identified as having less calcium than required. It has been determined as one of the risk factors not only in this study but also in other Asian studies involving the Chinese, Malaysian, Singaporean, Thai and Philippino populations.^{16,26} A European study has shown that the risk of hip fracture increases with diminishing calcium intake in subjects whose daily intake was <500 mg. In an Asian study, it was also found that diet calcium intake < 498 mg/d increases the risk of hip fracture. But in multivariate analysis in this study, it was not included as a risk factor. So future study involving more population and quantitative assessment of dietary calcium is required. Given that dietary calcium intake in most Asian countries is low; calcium supplements should have a considerable

impact on the reduction of osteoporotic fracture risk. Like physical activity, this variable is of great importance with respect to public health measures that can decrease the likelihood of osteoporotic fractures and thus relieve much of the morbidity and mortality associated with this condition in the Bangladeshi population. Much like calcium, adequate vitamin D is essential for bone strength, though it was not assessed in this study. Since vitamin D3 (with calcium) has been shown to reduce the risk of hip fractures in other elderly populations²⁷ and the fact that the Indian sub-continent population is considered Vitamin D deficient,²⁸⁻³⁰ the effect of sunlight and other vitamin D containing foods should be examined for their effect on osteoporotic fracture incidence. The effect of caffeine was estimated mainly by the consumption of tea- an extremely popular beverage with the Bangladeshi population and coffee. But no association with osteoporotic fracture was found in this study. It is also important to separate subjects based on the quantity of milk in their tea as some individuals may enjoy black tea and others may like to add milk. In Bangladesh, the majority prefer to add milk, albeit in varying amounts to their tea. Although previous research indicates that the effect of habitual tea drinking on bone density is minor and does not significantly alter the risk of fractures in an American population,³¹ this particular variable may be significant in the Bangladeshi population as 39.2% of the cases and 38.0% of the controls were regular tea/coffee drinkers. In many studies, a wide variety of medical conditions (e.g., multiple sclerosis, stroke, trauma-induced immobilization) and medications (e.g., immunosuppressant, oral glucocorticoids) were found to be associated with excess bone loss and fracture risk.^{24,25,32} In this study, rheumatoid arthritis, chronic kidney disease, immobilization, use of steroids, thyroid medication and loop diuretics were identified as risk factors which are consistent with the previous studies. The most important risk factor for fracture, independent of bone mineral density, is a previous fragility fracture. This history increases the risk of future fractures by as much as a factor of 8; the risk is highest in the first year or two after the initial episode.^{33,34} Silent vertebral fractures (identified radiologically) also increase the risk and should be looked for in patients who have lost more than 2 cm of height.³⁵ These two risk factors, e.g. previous history of fracture and loss of height along with family history of osteoporosis found significant in this study, may be used in mass population as screening for osteoporosis in a country like Bangladesh where most of the people are very poor to do any kind of laboratory test, let alone BMD. But a major limitation of the study is the relatively limited

sample size which impacted the power to detect the effect of certain variables deemed relevant by previous literature such as alcohol consumption (none in case and control group), smoking and hormone replacement therapy (none in both group). Unlike many other studies, early or immature menopause, either physiologically or surgically, was not found significant in this study.

It is also important to mention that as with all case control investigations, there is a possibility of recall bias and it is not possible to validate the information provided by the subject. However, given these constraints, valuable information was retrieved from the analysis.

Unlike many previous studies that focused on women, this investigation included both males and females. The distribution of hip fracture by age and sex was found to be different from that in the western counterparts studied in other investigations.^{18,19,30} Notwithstanding the high prevalence of osteoporosis and related fragility fractures in Bangladesh, and the resulting morbidity and mortality associated with the condition, there is no prior existing research on the risk factors of osteoporotic fractures in the Bangladeshi population. Given this formidable public health problem, the results of this study may be beneficial on a national level.

Conclusion:

This study has demonstrated some risk factors associated with osteoporotic fracture such as use of steroid and loop diuretics, arthritis, family history of osteoporosis and loss of height. But some known risk factors for osteoporotic fracture, e.g. lack of physical exercise, immobility, inadequate intake of diet rich in calcium content, caffeine, smoking, immature menopause, etc. were not found statistically significant in this study may be due to small study sample, selection bias or recall bias. Again this study may not represent the general population as it was done in hospital setting. So future study at the community level with larger sample size is recommended to find out the actual risk factors of osteoporotic fracture in the Bangladeshi population.

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