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The WHO FRAX Calculator with and without BMD as an Indicator of Low BMD in Pakistani Women

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Authors' contributions

This work was carried out in collaboration between all authors. Author MS designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors MS and MN did the data collection. Author NH revised the draft and gave the final approval. Authors MS and NH did the statistical analysis. Authors SS and RH provided the clinical input. All authors read and approved the final manuscript.

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ABSTRACT

Aims: BMD (bone mineral density) testing facilities are still scarce in Pakistan. We evaluated the predictive ability of FRAX with BMD (FRAX+) and FRAX without BMD (FRAX-) in a set of Pakistani females to assess their role in BMD assessment.
Study Design: Cross Sectional.
Place and Duration of Study: Department of Nuclear Medicine, Ziauddin hospital, Clifton Campus, Karachi, Pakistan between March and August 2016.
Methods: We enrolled 200 females above 40 years of age. Average age was 60.7 years (±10.52). Gold standard Dual Energy Xray Absorptiometry (DXA) scans were obtained to assess presence of low BMD. FRAX calculations with and without addition of femoral neck BMD were done. Statistical Package for Social Sciences (SPSS) version 20 was used to plot Receiver Operating

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Characteristics (ROC) and Area under Curve (AUC) was utilized for evaluation of tool's diagnostic accuracy.
Results: FRAX+ and FRAX- had comparable predictive power having AUC of 0.784 and 0.799 respectively. The Major Osteoporotic (MO) and hip fracture probabilities for FRAX+ and FRAX- showed significant correlation at the 0.001 level.
Conclusion: FRAX- may be utilized to assess BMD status in the absence of DXA facilities and to assess its need to avoid unnecessary scanning.

Keywords: FRAX; osteoporosis; fracture probability; risk assessment; Pakistan.

1. INTRODUCTION

Fragility fractures have strong relation to low bone mineral density [1,2]. However, it is now widely accepted that fragility fractures are caused by a multitude of risk factors. Low BMD may be the strongest but is not the sole predictor for assessing fracture risk [3]. This fact has been proved by the observation of a large proportion of fragility fractures occurring in people with BMD values in the osteopenic range compared to individuals with osteoporosis [4,5]. Advancing age, post-menopausal status, family history of osteoporosis, steroid use, cigarette smoking and alcohol intake are among the many determinants that affect bone strength [6,7]. Based on these observations the WHO designed a risk assessment tool, FRAX. This is a web based tool which computes the ten year probability of a major osteoporotic (MO) or a hip fracture. This probability may be computed with or without the use of femoral neck BMD [8]. FRAX has been incorporated in many national guidelines and has support of international bodies including International Osteoporosis Foundation (IOF), National Osteoporosis Foundation (NOF) and the International Society for Clinical Densitometry (ICSD) [9].

For utilization of the FRAX tool for risk estimation certain important points should be considered. The use of a country specific model and specific intervention threshold is essential. Fracture probabilities differ widely across the globe and the country specific models have been customized to individual fracture incidences and health policy dynamics of that particular country. If there is no FRAX model for any country then a representative surrogate country with similar fracture incidence should be chosen [4]. Till recently no data relevant to the South Asian population was included in FRAX. However, data of Singaporean patients of Indian ethnicity can now be used to calculate 10 yr probability of fracture risk, using FRAX. This newly updated version of FRAX is applicable to India and Pakistan, due to similarity in epidemiology of fragility fractures [10]. Age specific intervention thresholds have been proposed for interpretation of the Indian FRAX model. This approach is also being used in France, Switzerland, Europe, and UK and has been found to be cost effective [11].

Currently the diagnosis of osteoporosis is based on BMD values. Central DXA testing facilities are still scarce in the developing world. In this scenario the predictive ability of FRAX to identify high risk individuals may be employed and necessary interventions offered. Thus, the aim of this study was to compare the effectiveness of FRAX without BMD to FRAX with BMD and to find the correlation of their risk probabilities.

2. METHODOLOGY

This was a cross sectional study conducted in the Nuclear Medicine Department of Ziauddin Hospital, Karachi (Pakistan) from March to August 2016. Consecutive sampling technique was utilized to recruit 200 females from the Gynecology OPD of Ziauddin Hospital. Pre and postmenopausal females having natural menopause were included. Patients with prior diagnosis of osteoporosis, history of oophorectomy, hysterectomy or bone metastasis were excluded.

2.1 Measurements

Height, weight and BMI were recorded of all participants after taking their informed written consent. Participants were interviewed regarding information to be entered in the FRAX algorithm. These independent risk variables include prior fragility fracture, parental hip fracture history, current smoking, oral glucocorticoids long-term use, rheumatoid arthritis, other secondary causes of osteoporosis and alcohol consumption.

DXA scans were obtained using Hologic Discovery Wi (S/N 88577) DXA Scanner. Subjects were categorized into low and normal

BMD categories on the basis of femoral neck T scores according to the International Society for Clinical Densitometry (ISCD) guidelines [12]. Z scores were used for premenopausal females and T scores for postmenopausal females according to WHO recommendations [13] (Table 1).

2.2 FRAX Calculations

Fracture risk was calculated by entering participants' data in the FRAX online calculator (www.shef.ac.uk/FRAX). BMD femoral neck obtained from DXA scans were entered in the FRAX algorithm to calculate the FRAX with BMD values. The FRAX calculator computes fracture probability in terms of risk of major osteoporotic fracture (ie, hip, spine, wrist, and humerus) or hip fracture alone. Thus, we obtained FRAX without BMD(FRAX-) and FRAX with BMD (FRAX+) values for major osteoporotic and hip fractures for all participants. Age specific intervention thresholds endorsed by the Indian menopause society were utilized for categorizing participants as having either high or low fracture probability according to FRAX results. These thresholds have also been recommended by Prof. John A Kanis who headed the WHO task force for FRAX development (Fig. 1) [11].

2.3 Statistical Analysis

SPSS version 20 was used to analyze the data. Sample characteristics were defined in terms of means, standard deviations, frequencies and percentages. Receiver-operating-characteristic (ROC) analyses using area under the curve (AUC) was used to evaluate the overall ability of FRAX- and FRAX+ to predict fracture risk based on BMD T-score categories (normal, and low bone mass).

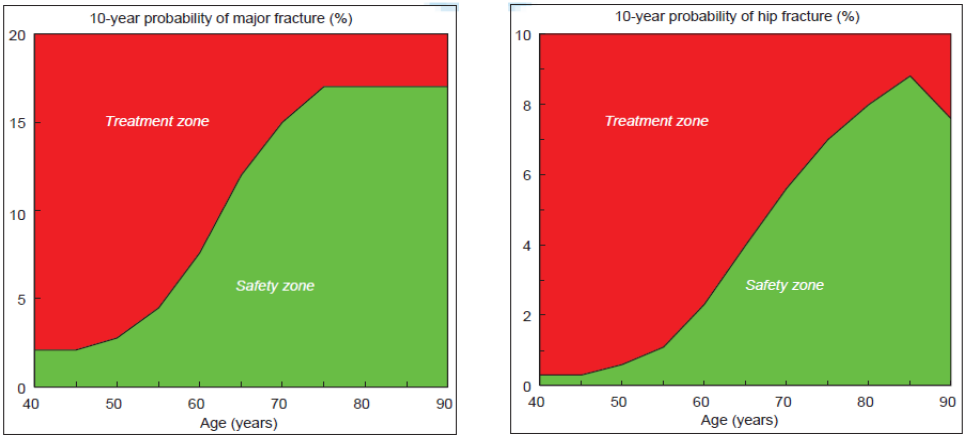
After running the normality test on data Pearson correlation was applied. Correlation of risk probabilities obtained for Major Osteoporotic fracture and Hip fracture by the FRAX- and FRAX + was found. Correlation results were graphically represented by scatter plots.

3. RESULTS

The average age of our sample was 60.7(±10.52) years, ranging from 40 to 93 years. According to femoral neck BMD 111 women (55.5%) had low BMD (T score<–1 for postmenopausal and Z score <-2 for premenopausal women). 89 women (44.5%) had normal BMD (T score >–0.9 for postmenopausal and Z score >-2 SD for premenopausal females).

Table 1. Categorization of DXA results

Pre menopausal women		Post menopausal women	
Normal	Z score upto -1.9 SD	Normal	T score ≥ -1 SD
Low BMD	Z score ≤ -2 SD	Low BMD	T score < -1



(a) **(b)**

Fig. 1. (a) Major Osteoporotic Fracture threshold (b) Hip fracture threshold. "Fracture threshold" denoted by the sigmoid curve, the red zone represents high fracture risk and green area represents low fracture risk (Image used with permission of the Centre for Metabolic Bone Diseases, University of Sheffield. FRAX® is registered to Professor JA Kanis, University of Sheffield)

Table 2. Study participants' characteristics

Variables	Mean±SD	Minimum	Maximum
Age of Patients (years)	60.76±10.52	40	93
Height (cm)	155.02±6.33	135	170
Weight (kg)	69.25±15.32	29	125
BMI (kg/m^2)	28.74±5.79	15.90	45.50
BMD Femoral Neck (g/cm^2)	0.7286±0.14	0.26	1.15
T-score femoral Neck	-1.05±1.217	-5.30	2.70

Fig. 2 represents the Receiver Operating Characteristics curve plotted for FRAX- and FRAX + values at femoral neck T score<-1 indicating individuals with low BMD. The diagnostic accuracy of a tool is represented by AUC and ranges from 0.5 for a non-informative tool to 1.0 for perfect concurrence. An AUC of 0.7 represents good accuracy. The AUC obtained for FRAX- and FRAX + are shown in Table 3. The AUC was above 0.7 for both FRAX + and FRAX – indicating comparable performance in our sample for detecting low BMD.

We examined the relationship between the ten year MO fracture risk probabilities obtained by FRAX- and FRAX+ and that between hip fracture probabilities obtained by FRAX- and FRAX+. There was considerable agreement between them. On applying Pearson's correlation the correlation coefficients were r = 0.825 for MO probabilities with and without BMD and r = 0.759 for hip fracture probabilities respectively. The scatter plots show strong positive correlation between the FRAX- and FRAX+ values for both probabilities. (Fig. 3)

Table 3. AUC values for FRAX+ and FRAX-

Tools	Area under the curve
FRAX without BMD (FRAX-)	0.799
FRAX with BMD (FRAX+)	0.784

4. DISCUSSION

The aim of our study was to evaluate the impact of including Femoral Neck (FN) BMD values on the FRAX calculation in a set of Pakistani females. Females with low BMD at the femoral neck have been found to be at high risk of suffering from fragility fractures [14]. It has been debated that persons in the osteopenic range are at increased fracture risk since osteopenia and not osteoporosis accounts for high frequency of fragility fractures [4].

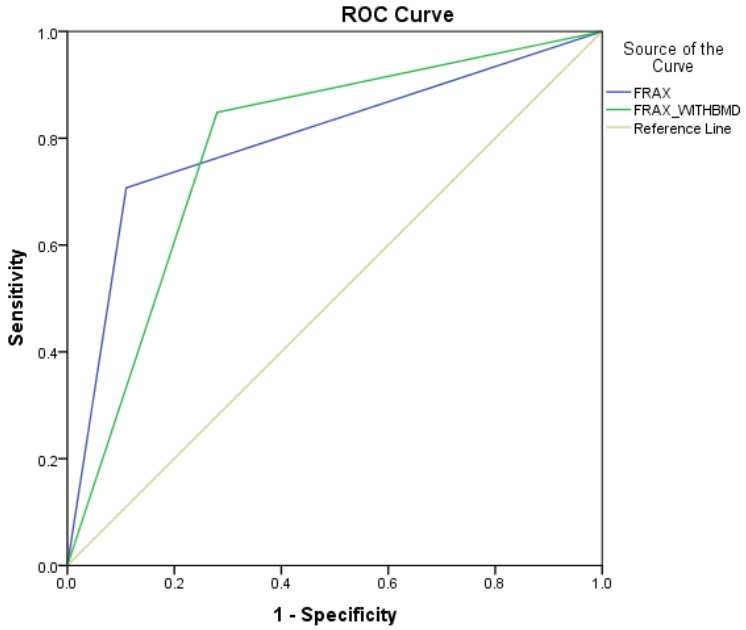
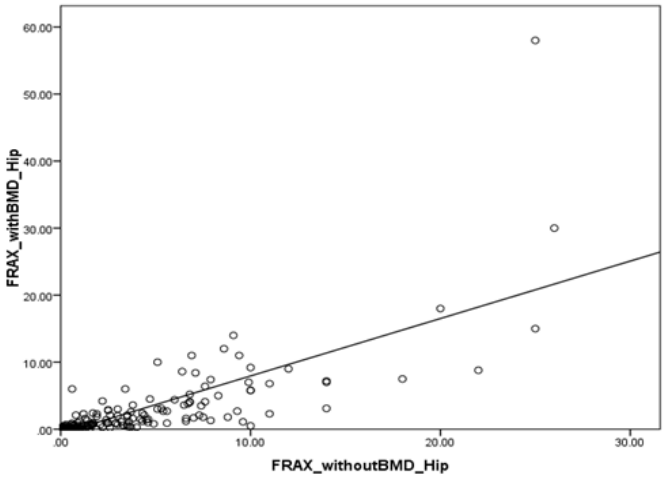
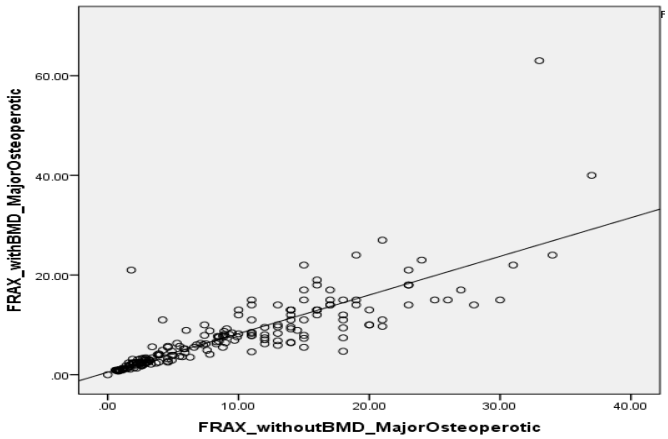


Fig. 2. Receiver operating characteristics based on femoral neck T score<-1 (low BMD)



(a)



(b)

Fig. 3. Scatter plot graph of agreement between FRAX estimated 10-year fracture probabilities with and without the inclusion of BMD results (a) hip fracture (b) MO fracture

Pakistan faces health care challenges because of underdeveloped health care systems and unequal distribution of resoursces [10]. In Pakistan 9.91 million people (7.19 million women and 2.71 million men) are affected by osteoporosis, and these numbers are estimated to rise to 11.3 million by 2020 [15]. In spite of the high prevalence of this disease there are no national statistics available for hip fracture incidence in this country. To add to the problem, a scarcity of DXA machines has been reported across the country [15]. Such issues impede the timely diagnosis of this disease thus missing opportunities of fracture prevention. The International Osteoporosis Foundation in its Asian Audit in 2013, emphasized the need of action plans for prevention, treatment, diagnosis and fracture care in Pakistan [16] Leena Jaferi et al recently pointed out differences in the prevalence of certain risk factors eg. alcohol usage in Pakistani Muslim population compared to other ethnicities. Alcohol use is one of the factors included in FRAX calculations. It has thus been stressed that osteoporosis risk assesment tools be tested in Pakistani population and their diagnostic accuracy determined [17].

We found FRAX to have good diagnostic accuracy in identifying females with low BMD. The AUC values obtained for FRAX with and without BMD were above 0.7 indicating that this tool can be utilized for screening purposes. Our results show slightly better performance of the FRAX calculator without BMD than that of FRAX with BMD. This is similar to results reported by Abdellah et al. who conducted a cross sectional

study on Moroccan females and found better performance of FRAX without BMD [18]. Previous studies reporting the impact of BMD to FRAX calculations have shown mixed results. Researches conducted in the United States and Turkey have reported comparable results for FRAX calculations with and without BMD [19,20]. A recent study from India conducted by Bhavna et al. in 2016 reported discordance in FRAX calculations on inclusion of BMD [21]. We on the contrary have reported comparable calculations for FRAX+ and FRAX-. This difference in our results may be due to the fact that we have utilized country specific and age specific intervention thresholds for FRAX interpretation while Bhavna et al. have used fixed thresholds.

We also found significant positive correlation between MO and hip fracture probabilities calculated with and without BMD inclusion. This correlation was found to be more significant for MO then for hip fractures. Our findings are comparable to those reported by Nese et al. on Turkish females and by Yasmin et al. on Brazilian females [20,22]. This shows that that there is considerable agreement between the fracture probabilities with and without BMD addition to the calculation.

On the basis of our results it may be proposed that in case of non-availability of BMD testing facilities FRAX tool can be utilized for BMD assesment. This approach may prove extremely beneficial for the struggling health care system of Pakistan. Previous studies have also proposed that FRAX may be utilised in areas where BMD facilities are scarce [23,24].

To the best of our knowledge this is the first study assessing FRAX performance in Pakistan. We recruited our study participants from a tertiary care hospital and thus the sample may not be representative of the general population. This may be considered as a potential limitation. Future studies with follow up designs are recommended to compare the power of FRAX prediction to actual fracture incidences.

5. CONCLUSION

We conclude that a pre BMD FRAX can efficiently predict treatment need in those at risk. Thus FRAX without BMD is appropriate for use in community as well as outpatient departments and may prove helpful in lowering the unnecessary use of DXA.

ETHICAL APPROVAL

Ethical approval was obtained from Ethics Review Committee of Ziauddin University, Karachi, Pakistan.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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