

ORIGINAL ARTICLE

The impact of the Hologic vs the ICMR database in diagnosis of osteoporosis among South Indian subjects

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Summary

Background and Objectives Recently, the Indian Council of Medical Research (ICMR) has published normative data for bone mineral density (BMD) measured by dual-energy X-ray absorptiometry (DXA) scanning. However, the impact this has had on the diagnosis of osteoporosis when compared to currently used Caucasian databases has not been analysed. Hence, this study was undertaken to look at agreement between the Hologic Database (HD) based on BMD normative data in Caucasians and the ICMR database (ICMRD) in defining osteoporosis in subjects with or without hip fracture.

Materials and Methods It is a cross-sectional study of 2976 subjects (men 341, women 2757) (mean age \pm SD = 62.2 \pm 7.2 years), including 316 subjects with low impact hip fracture: 2199 were from the hospital database, and 461 were healthy postmenopausal women from the community who underwent (DXA) scanning between January 2010 and March 2013. Recalculated *T* scores from ICMRD were used for the diagnosis of osteoporosis and compared with HD.

Results An almost perfect agreement existed between the two databases for the diagnosis of osteoporosis at the hip (κ -0.82, $P < 0.0001$) in all subjects, and a moderate relationship existed in those with hip fracture (κ -0.65, $P < 0.0001$). Seventy-three of 316 hip fracture subjects (23.5%) defined as osteoporosis according to HD were classified as osteopenia according to ICMRD.

Conclusion The threshold of hip BMD *T* score for treating osteoporosis may have to be redefined if the ICMR reference database is used. Initiation of treatment in these subjects must be based on multiple fracture risk factor assessment in addition to looking at BMD. Further studies with a larger sample size of subjects with fracture are needed to validate our findings.

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Introduction

Osteoporosis is the common metabolic bone disease, which has a significant economic burden globally. The current population-based prevalence of people with low bone mineral density in the United States is 57 million, as demonstrated in the most recently released data by the National Osteoporosis Foundation, which also showed a huge variation in the prevalence among different ethnicities.¹ India is one of the largest affected countries in the world where one out of every eight men and one out of every third woman has osteoporosis.² An earlier peak incidence of osteoporosis has also been reported in Indians as compared to the western subjects who usually develop it one to two decades later.^{1,2}

Peak bone mass (PBM) is the maximum bone mass present at the end of skeletal maturation which is acquired by third decade of life. The PBM depends on genetic, nutritional and other environmental factors and thus differs in different ethnicities.³ These factors may explain the variations seen in the bone mineral density (BMD) across different adult populations. The dual-energy X-ray absorptiometry (DXA) remains the main diagnostic modality for diagnosing osteoporosis.⁴ The current DXA machines have incorporated Caucasian-based BMD as normative data for the diagnosis of low bone mass. For example, the reference database used in the Hologic machine is based on the data from 14 646 men and women, nationally representative U.S. adults collected during the National Health and Nutrition Examination Survey III (NHANES-III, 1988–94).⁵

The relevance of using Caucasian reference database for diagnosing osteoporosis in other populations has been questioned in view of ethnic differences in attainment of peak bone mass. Also, most published Indian studies have shown a low bone mass across all age groups. This necessitated the Indian Council of Medical Research (an apex body in India for conducting medical research) to derive a reference data for bone mineral density. This was a multicentre study conducted between 2001–2006 to arrive at the reference BMD at hip, forearm and spine in healthy Indian individuals ($n = 808$) aged 20–29 years.⁶

However, the performance of ICMR database in comparison with Caucasian database in categorizing BMD into various groups has not been studied. So, we attempted to look at the agreement in classifying BMD by the *T* score derivations from Hologic Database (HD) and the Indian Council of Medical Research Database (ICMRD) in a south Indian semi-urban population. More

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importantly, we also looked at the agreement in diagnosis in a subset of population who had sustained a hip fracture.

Making an appropriate diagnosis of osteoporosis and thereafter providing corrective measures to the affected individuals has shown definite benefit to prevent mortality in these subjects.⁷

Material and methods

This is a cross-sectional study of subjects ($n = 2976$) who underwent assessment of bone mineral density at the hip between January 2010 and March 2013 at a South Indian tertiary care institution. This study was approved by institutional review board. Study subjects comprised of three groups. Group A included subjects with low impact hip fracture (fracture subjects) who underwent DXA scan in the unaffected hip within 48 h of sustaining fracture. Group B comprised of hospital subjects who were referred for DXA for indications other than fracture (hospital data). As hospital subjects may be not a true representative of community, healthy postmenopausal women were recruited, who constituted the group C (community data).

Data regarding age, sex and BMD were collected. T scores of hip according to both Hologic and ICMR database were computed using the following formula:

$$T - \text{Score} = \frac{\text{Patient BMD (gm/cm}^2\text{)} - \text{Young adult reference BMD (gm/cm}^2\text{)}}{\text{SD (gm/cm}^2\text{)}}$$

The WHO categorization of BMD was used to define osteoporosis.⁸

Bone mineral density was assessed using Hologic QDR 4500 Discovery-A densitometer. Weighted κ was used to look at the agreement between the two databases in categorizing BMD into normal, osteopenia and osteoporosis at hip in overall and in subjects with hip fracture. The κ values were scaled as no agreement if <0 , 0–0.20 as slight, 0.21–0.40 as fair, 0.41–0.65 as moderate, 0.66–0.80 as substantial and 0.81–1 as almost perfect agreement. The sample size required to be studied for an expected agreement of 0.6 with an 80% power and 5% level of significance was 551 subjects. SAS Version 9.1.3 (SAS Institute, Cary, NC) was used for data analysis.

Results

The total number of subjects studied were 2976 (341 men, 2757 women) of which group A (fracture subjects) were 316, group B (hospital data) were 2199 and group C (community data) were 461. The mean age (\pm SD) of these subjects was 62.2 (\pm 7.2) years. There was no significant difference with regards to age between the three groups ($P = 0.56$). The first two groups comprised of 89% women.

The categorization of subjects into normal, osteopenia and osteoporosis according to HD and ICMR database (ICMRD) is given in Table 1.

Of the 2976 subjects, 1314 (44%) and 1580 (53%) were classified as normal and 1267 (42%) and 1091 (36.6%) as osteopenia

Table 1. Distribution of hip one mineral density (BMD) according to Hologic database and Indian Council of Medical Research database (ICMRD)

Hologic database	ICMR database			Total
	Normal	Osteopenia	Osteoporosis	
Normal	1307	1	6	1314
Osteopenia	271	994	2	1267
Osteoporosis	2	96	297	395
Total	1580	1091	305	2976

The shaded values are weighted Kappa -0.82 ; CI $-0.80-0.83$, almost perfect agreement.

according to Hologic and ICMR databases, respectively. Osteoporosis was diagnosed in 395 (13.2%) and 305 (10.2%) subjects as per HD and ICMRD, respectively.

Twenty per cent of cases categorized as osteoporosis by the Hologic database were reclassified as osteopenia by ICMR database (Figure 1).

Among the subjects with hip fracture, 193 (61%) were classified as osteoporosis based on the HD while 120 (38%) by the

ICMR database. Seventy-three of 316 hip fracture subjects (23%) defined as osteoporosis according to Hologic data were reclassified as osteopenia according to ICMR database (Figure 2). There was a significant correlation between the T scores computed by the ICMR database and Hologic database in overall subjects ($R = 0.8$, $P = 0.001$), (Figure 3a). A Bland–Altman plot for

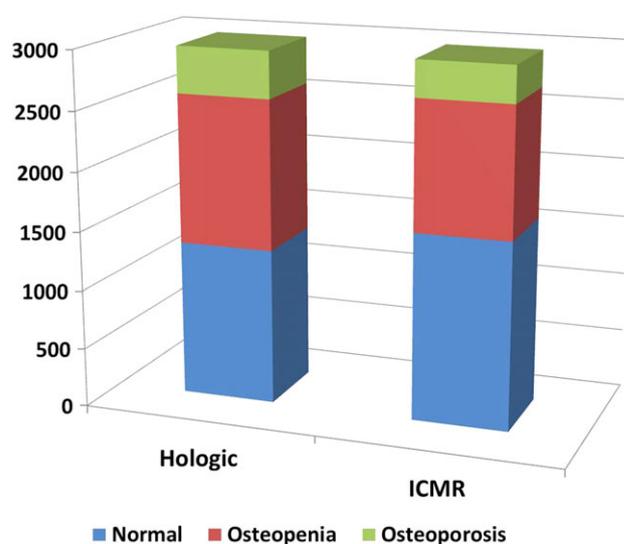


Fig. 1 Reclassification of severity of low bone mineral density based on Hologic Database vs Indian Council of Medical Research database (ICMRD).

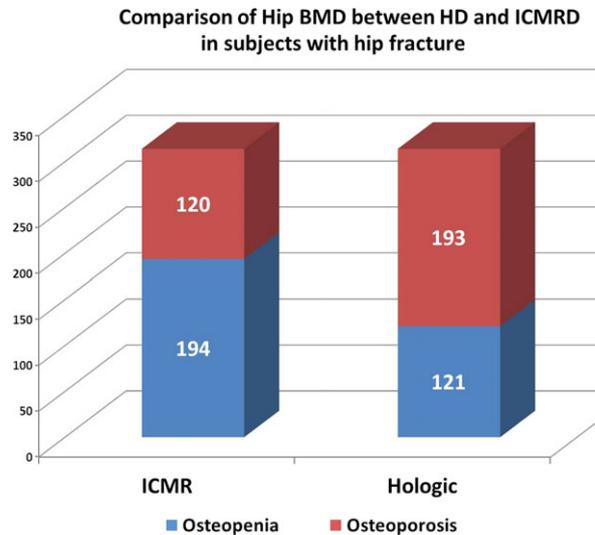


Fig. 2 Reclassification of the severity of low bone mineral density in subjects with hip fracture based on Hologic Database vs Indian Council of Medical Research database (ICMRD).

looking at an agreement between both Hologic and ICMR T scores showed that most of the points were within the 95% confidence interval (0.34 to -0.98), thus revealing a good agreement (Figure 3b).

The agreement between the two databases was almost perfect with weighted κ of 0.82 (CI 0.80–0.83) for overall subjects and was moderate with a weighted κ of 0.65 (CI 0.62–0.67) in categorizing subjects with low impact hip fracture.

Discussion

This study highlights the fact that the choice of normative data for categorizing BMD in a particular ethnic population may have an impact on reclassifying the severity of low bone mineral

density. The HD and ICMRD were in ‘almost perfect’ agreement with each other for diagnosing osteoporosis at the hip in the whole cohort and in moderate agreement in subjects who had sustained hip fracture.

Reference peak BMDs (PBMD) of the femoral neck according to the HD are 1.041 ± 0.054 gm/cm² (men) and 0.941 ± 0.122 gm/cm² (women).⁵ Low PBMD established in ICMRD [0.988 ± 0.131 gm/cm² (men) and 0.901 ± 0.111 gm/cm² (women)]⁶ may explain the difference we found in categorizing into various groups.

Overall, studies from various parts of the Indian continent have described a low peak bone mass contributed by differences in skeletal size, a high prevalence of vitamin D deficiency and genetic variations. This results in an ethnicity-specific lower bone mass in Indian subjects thereby making the control reference population itself to have a low baseline bone mineral density. This further narrows the gap between severe bone disease and normal Indian subject, resulting in a much smaller standard deviation (T score) in some subjects with severely affected bone disease. In line with these results, we derive that in subjects with hip fracture, ICMR database may reclassify certain group of people as having osteopenia despite actually having osteoporosis.

There is a large regional variation in the reported incidences of hip fracture across the globe. A higher incidence has been reported in northern Europe and in the United States followed by Asian countries such as Kuwait, Iran, China and Hong Kong and lowest in Latin America and Africa. In India, the reported incidence of hip fracture above 50 years of age is 129/100 000. This is probably due to differences in latitude, genetics, ethnicities and environmental factors.^{9,10}

The effect of using Indian-based reference standards for calculating T scores and BMD classification in South Asian Indians seen in our study concurs with an earlier finding that differences in ethnicities have an impact on the diagnosis of osteoporosis.^{9,11} At this point, it is prudent to use the Hologic Database

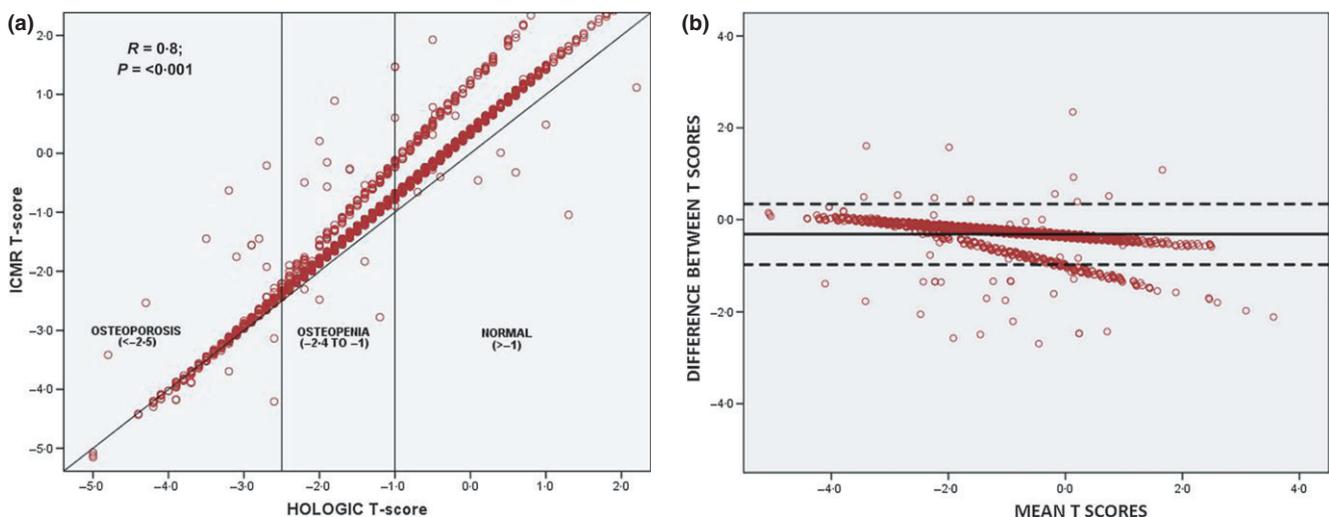


Fig. 3 (a) Correlation between Hologic Database and Indian Council of Medical Research database (ICMRD) T scores (osteoporosis ≤ -2.5 , osteopenia = between -1 and -2.5 , normal ≥ -1). (b) Bland–Altman plot showing the agreement between Hologic Database and ICMRD T scores (mean = solid line and 2 SD = dotted lines).

rather than ICMRD, as the later seems to underestimate the problem until further prospective studies are available to validate our findings.

However, despite having low BMD, the incident fracture rates are comparatively less in Indians.⁷ It is not clearly known why the fracture rate is low in spite of having higher prevalence of osteoporosis. It has been noted that several risk factors predispose to hip fractures, independent of BMD. Hence, use of a fracture risk assessment tool like FRAX may help in better management of these patients. Our study is limited by the fact that only a small number of patients were included in the hip fracture group.

Conclusion

In our study, the Indian ethnicity-based database diagnosed lesser number of subjects to have osteoporosis when compared to Caucasian reference population. However, initiation of treatment in this group of subjects must be based on multiple risk factor assessment in addition to looking at the BMD. Further studies with a larger sample size of subjects with fracture are needed to validate our findings.

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