Short Communication

Effect of parity on phalangeal bone mineral density in post-menopausal Sri Lankan women: a community based cross-sectional study

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Abstract

There is paucity of studies related to parity and bone mineral density in South Asian countries. We recruited 713 healthy, community dwelling post-menopausal women from seven provinces in Sri Lanka for this survey. The number of pregnancies, including miscarriages beyond 20 weeks of gestation, was recorded. Women with diseases and those who have taken drugs that can affect bone mineral density (BMD) were excluded ($n = 15$). Phalangeal BMD and bone mineral content (BMC) were measured using AccuDEXA in 713 women. Mean (SE) BMD of nulliparous women ($n = 32$), women with one to two pregnancies ($n = 284$), three to four pregnancies ($n = 290$) and more than four pregnancies ($n = 107$) were 0.437(0.014), 0.454(0.005), 0.455(0.005) and 0.417(0.006) g/cm², respectively ($P < 0.001$). Corresponding mean (SE) BMCs were 1.30(0.063), 1.41(0.021), 1.43(0.022) and 1.32(0.033) g, respectively ($P < 0.001$). Women with more than four pregnancies were older and lighter when compared with other groups. When results were adjusted for current age and current weight, differences in mean BMD and BMC between groups became non-significant. BMD of nulliparous women remained low in all analyses. We report a significant difference in unadjusted phalangeal BMD in women categorized according to their parity. Women with one to four pregnancies had the highest phalangeal BMD and BMC, while multi-parous (more than four pregnancies) and nulliparous women had lower values. However, in an adjusted analysis, the differences in BMD and BMC were partially explained by the differences of age and body weight between the groups and the unique effect of parity was difficult to determine. Women with lower BMD may have a higher risk of future fractures.

Keywords: AccuDEXA, phalangeal BMD, Sri Lanka, parity.

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Introduction

Osteoporosis and fragility fractures have become a major health problem worldwide and more osteoporosis-related fractures are expected in Asian countries (Cooper *et al.* 1992). Before the occurrence of a fracture, the diagnosis of osteoporosis is based on the bone mineral density (BMD) measured in the spine, proximal femur or forearm bones. Furthermore, BMD is used to estimate future fracture risk and monitor treatment efficacy (Kanis 2000). While genetic factors account for 70–80% variation in BMD (Pocock *et al.* 1987; Flicker *et al.* 1995), other factors such as age, sex, nutrition, social habits, physical activity and body measurements account for the balance 20–30% BMD variation (Flicker *et al.* 1995). Pregnancy and lactation induce a state of high bone turnover. During pregnancy, growing fetus utilizes about 25–30 g of maternal calcium for its skeletal development. This is followed by a loss of about 200 mg of calcium per day in breast milk during lactation (Prentice 2000). Furthermore, a lactating mother experiences a period of post-partum amenorrhea associated with hypoestrogenaemia which may last for about 8 months in some women. All of the above contribute to a negative calcium balance during pregnancy and lactation, leading to loss of BMD.

During pregnancy and lactation, many physiological adaptations operate to minimize the effects of high calcium demand on maternal skeleton. Fractional calcium absorption is increased during pregnancy nearly from 33% in the non-pregnant state to 50% in the second trimester, and to 55% in the third trimester, and these changes are parallel to the increase in serum 1, 25 vitamin D levels (Singh *et al.* 1999; Abrams 2003). Fractional calcium absorption and serum 1, 25 vitamin D level are increased during lactation while urinary calcium excretion is lower in lactating women than non-lactating controls, indicating increased renal calcium re-absorption during lactation (Prentice 2000). Ritchie *et al.* observed enhanced maternal intestinal calcium absorption during pregnancy while maternal urinary calcium excretion was low during early period of lactation. In the same group of 14 women, loss of spinal BMD was

evident during early lactation period but not during pregnancy (Ritchie *et al.* 1998).

Previous studies examining the effect of parity on BMD generated conflicting results. While some studies showed no association (Hamed *et al.* 1992; Kojima *et al.* 2002), others showed either positive (Cure-Cure *et al.* 2002; Sadat-Ali *et al.* 2005) or negative (Parra-Cabrera *et al.* 1996; Ghannam *et al.* 1999; Zhang *et al.* 2003) associations between parity and BMD. This probably reflects the differences in study populations with regard to number of children, breastfeeding practices, smoking habits, alcohol consumption, nutrition and the degree of physical activities. Most of the studies on parity and BMD are based on western populations or countries in Far East Asia and data on South Asian women are sparse. Some studies have indicated that women in South Asian countries are different from women in western countries or Far East Asia (Lean *et al.* 2001). Hence, the results of the studies done elsewhere cannot be directly applied to women in South Asian countries.

Epidemiological data related to bone health in South Asian women are limited. Restricted availability of dual energy X-ray absorptiometry (DXA) facility in South Asian countries may have contributed to the scarcity of epidemiological studies on BMD in these countries. This cross-sectional study was done to assess the effect of parity on BMD in a sample of post-menopausal women selected from seven provinces in Sri Lanka.

Methods

A group of community dwelling healthy women from seven out of nine provinces in Sri Lanka was recruited to the study. Two areas, one representing urban and one representing rural populations, were selected randomly, from each province. General public in selected areas was informed about the purpose of the study 2–3 days prior to the visit to the area. All volunteers gathered in scanning centres were included in the study.

All subjects filled in a health-related questionnaire, and their current body weight was measured while wearing light clothes and after removing footwear. The number of pregnancies, including miscarriages

of more than 20 weeks of gestation, was recorded. Phalangeal BMD and bone mineral content (BMC), in the middle phalanx of the middle finger of the non-dominant hand, were measured using AccuDEXA scanner (Schick Technologists, New York, USA). One technician measured all subjects included in this analysis while accuracy and precision of BMD and BMC estimations were verified each morning by scanning the inbuilt phantom. T- and Z-scores, for phalangeal BMD were calculated using the European white female reference data provided by the manufacturer (see formulae below). The manufacturer of AccuDEXA does not provide Asian female reference data and we were unable to find phalangeal BMD reference data from other Asian populations. Women with history of diseases such as renal failure, chronic liver disease, hyperthyroidism, hyperparathyroidism, malabsorption, chronic inflammatory arthritis or chronic diseases of inflammatory nature were excluded from the study. Women who had taken systemic corticosteroids, vitamin D, gonadal hormone replacement, anti-resorptives, pharmacological doses of calcium or anti-epileptics were also excluded from the analysis. Women with past history of fracture were not excluded from the study. Only the women who had complete data on parity and BMD ($n = 713$) were considered for this study. Details of the method of recruitment have been published earlier (Lekamwasam *et al.* 2007). Each subject signed a consent form, while Ethical Review Committee of the Faculty of Medicine, Galle, gave the ethical approval for the study.

$$\text{T-score} = \frac{\text{Subject's BMD} - \text{mean BMD of the young adult female population}}{\text{Standard deviation of the young adult female population}}$$

$$\text{Z-score} = \frac{\text{Subject's BMD} - \text{mean BMD of the age matched female population}}{\text{Standard deviation of the age matched female population}}$$

Statistical analysis

Correlations between BMD, BMC, current age and current weight were examined by Pearson correlation

coefficient. Women were categorized according to the number of pregnancies; Group 1: nulliparous, Group 2: 1–2 pregnancies, Group 3: 3–4 pregnancies, Group 4: more than 4 pregnancies. Phalangeal BMD, BMC, T- and Z-scores in the subgroups were compared, first unadjusted and then adjusted for current age and current weight using ANCOVA. Post hoc test with Bonferroni correction was used to test differences between groups. No significant interactions between variables, current age and weight were found during the analysis. Similarly, above variables showed no interactions with subgroups of women categorized according to parity. Data were not adjusted for smoking or alcohol consumption as only 0.8% of women were found to have taken alcohol or smoked ever in their life. Furthermore, data were not adjusted for the period of breastfeeding as this was not inquired from all subjects in detail. $P < 0.05$ was taken as the level of statistical significance and SPSS version 10 (SPSS Inc., Chicago, IL) for Windows was used for all analyses.

Results

The number of pregnancies varied from 1 to 14 with median (inter quartile range) of 3 (2–4). Age showed negative correlations with BMD and BMC ($r = -0.49$ and -0.39 , respectively, $P < 0.001$ for both) while body weight showed positive correlations with BMD and BMC ($r = 0.37$ and 0.35 , respectively, $P < 0.001$ for both). Women with more than four pregnancies (Group 4) were older and lighter when compared with women in other groups (Table 1). The age at menopause was not significantly different between groups.

The highest phalangeal BMD and BMC were found in women who had one to four pregnancies (Groups 2 and 3). Nulliparous and multi-parous (more than four pregnancies) women had lower phalangeal BMD and BMC compared with other groups. This trend was seen in unadjusted T- and Z-scores. When the model was adjusted for current age, the above pattern was less marked but still remained statistically significant. When current age and current weight were included in the model, the differences were no longer statistically significant. Inclusion of the years since menopause did not change the results

Table 1. Descriptive data of 713 women categorized according to parity

Variable	Group 1 (n = 32)	Group 2 (n = 284)	Group 3 (n = 290)	Group 4 (n = 107)	P*
Current age: years	54.4 (1.37)	54.6 (0.47)	56.1 (0.47)	60.0 (0.72)	<0.001
Current weight: kg	53.2 (1.93)	55.5 (0.65)	58.6 (0.66)	52.2 (1.01)	<0.001
Age at menopause: years	48.5 (0.99)	47.3 (0.34)	47.7 (0.34)	46.2 (0.54)	0.054

Group 1, never pregnant; Group 2, one to two pregnancies; Group 3, three to four pregnancies; Group 4, more than four pregnancies. *P contrasts differences of mean values in four groups and assessed by ANOVA with Bonferroni correction. Age, weight and age at menopause are given as mean and standard errors (within brackets).

Table 2. Unadjusted and adjusted BMC, BMD, T-score and Z-score of 713 women in four subgroups

Variable		Group 1 (n = 32)	Group 2 (n = 284)	Group 3 (n = 290)	Group 4 (n = 107)	P [‡]
BMD (g/cm ²)	*	0.437 (0.014)	0.454 (0.005) ^a	0.455 (0.005) ^a	0.417 (0.006) ^b	<0.001
	**	0.435 (0.011) ^c	0.451 (0.004)	0.461 (0.004) ^d	0.444 (0.007) ^c	0.034
	***	0.437 (0.012)	0.451 (0.004)	0.453 (0.004)	0.444 (0.007)	0.44
BMC (g)	*	1.30 (0.063)	1.41 (0.021)	1.43 (0.022)	1.32 (0.033)	<0.001
	**	1.31 (0.053)	1.41 (0.018)	1.45 (0.018)	1.40 (0.030)	0.050
	***	1.31 (0.058)	1.41 (0.019)	1.41 (0.019)	1.40 (0.031)	0.48
T-score	*	-1.46 (0.276)	-1.14 (0.094)	-1.12 (0.095)	-1.85 (0.146)	<0.001
	**	-1.51 (0.220)	-1.20 (0.075)	-1.01 (0.074)	-1.34 (0.125)	0.034
	***	-1.47 (0.239)	-1.19 (0.078)	-1.15 (0.078)	-1.33 (0.126)	0.44
Z-score	*	-0.80 (0.175)	-0.54 (0.059)	-0.47 (0.060)	-0.80 (0.091)	0.014
	**	-0.79 (0.155)	-0.54 (0.053)	-0.42 (0.052)	-0.65 (0.089)	0.034
	***	-0.74 (0.169)	-0.53 (0.055)	-0.51 (0.055)	-0.632 (0.089)	0.44

BMC, bone mineral content; BMD, bone mineral density; Group 1, never pregnant; Group 2, one to two pregnancies; Group 3, three to four pregnancies; Group 4, more than four pregnancies; *Unadjusted; **Adjusted for current age; ***Adjusted for current age and current weight; [‡]P contrasts differences of mean values in four groups and assessed by ANOVA or ANCOVA with Bonferroni correction; ^a vs. ^b, ^c vs. ^d, ^e vs. ^f, ^g vs. ^h, ⁱ vs. ^j, ^k vs. ^l, ^m vs. ⁿ, ^o vs. ^p, ^q vs. ^r, ^s vs. ^t, ^u vs. ^v, ^w vs. ^x, ^y vs. ^z, ^{aa} vs. ^{ab}, ^{ac} vs. ^{ad}, ^{ae} vs. ^{af}, ^{ag} vs. ^{ah}, ^{ai} vs. ^{aj}, ^{ak} vs. ^{al}, ^{am} vs. ^{an}, ^{ao} vs. ^{ap}, ^{aq} vs. ^{ar}, ^{as} vs. ^{at}, ^{au} vs. ^{av}, ^{aw} vs. ^{ax}, ^{ay} vs. ^{az}, ^{ba} vs. ^{bb}, ^{bc} vs. ^{bd}, ^{be} vs. ^{bf}, ^{bg} vs. ^{bh}, ^{bi} vs. ^{bj}, ^{bk} vs. ^{bl}, ^{bm} vs. ^{bn}, ^{bo} vs. ^{bp}, ^{bo} vs. ^{bq}, ^{br} vs. ^{bs}, ^{bt} vs. ^{bu}, ^{bv} vs. ^{bw}, ^{bx} vs. ^{by}, ^{bz} vs. ^{ca}, ^{cb} vs. 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vs. ^{sv}, ^{sv} vs. ^{sw}, ^{sw} vs. ^{sx}, ^{sx} vs. ^{sy}, ^{sy} vs. ^{sz}, ^{ta} vs. ^{tb}, ^{tb} vs. ^{tc}, ^{tc} vs. ^{td}, ^{td} vs. ^{te}, ^{te} vs. ^{tf}, ^{tf} vs. ^{tg}, ^{tg} vs. th, th vs. ^{ti}, ^{ti} vs. ^{tj}, ^{tj} vs. ^{tk}, ^{tk} vs. ^{tl}, ^{tl} vs. tm, tm vs. ^{tn}, ^{tn} vs. ^{to}, ^{to} vs. ^{tp}, ^{tp} vs. ^{tq}, ^{tq} vs. ^{tr}, ^{tr} vs. ^{ts}, ^{ts} vs. ^{tt}, ^{tt} vs. ^{tu}, ^{tu} vs. ^{tv}, ^{tv} vs. ^{tw}, ^{tw} vs. ^{tx}, ^{tx} vs. ^{ty}, ^{ty} vs. ^{tz}, ^{ua} vs. ^{ub}, ^{ub} vs. ^{uc}, ^{uc} vs. ^{ud}, ^{ud} vs. ^{ue}, ^{ue} vs. ^{uf}, ^{uf} vs. ^{ug}, ^{ug} vs. ^{uh}, ^{uh} vs. ^{ui}, ^{ui} vs. ^{uj}, ^{uj} vs. ^{uk}, ^{uk} vs. ^{ul}, ^{ul} vs. ^{um}, ^{um} vs. ^{un}, ^{un} vs. ^{uo}, ^{uo} vs. ^{up}, ^{up} vs. ^{uq}, ^{uq} vs. ^{ur}, ^{ur} vs. ^{us}, ^{us} vs. ^{ut}, ^{ut} vs. ^{uu}, ^{uu} vs. ^{uv}, ^{uv} vs. ^{uw}, ^{uw} vs. ^{ux}, ^{ux} vs. ^{uy}, ^{uy} vs. ^{uz}, ^{va} vs. ^{vb}, ^{vb} vs. ^{vc}, ^{vc} vs. ^{vd}, ^{vd} vs. ^{ve}, ^{ve} vs. ^{vf}, ^{vf} vs. ^{vg}, ^{vg} vs. ^{vh}, ^{vh} vs. ^{vi}, ^{vi} vs. ^{vj}, ^{vj} vs. ^{vk}, ^{vk} vs. ^{vl}, ^{vl} vs. ^{vm}, ^{vm} vs. ^{vn}, ^{vn} vs. ^{vo}, ^{vo} vs. ^{vp}, ^{vp} vs. ^{vq}, ^{vq} vs. ^{vr}, ^{vr} vs. ^{vs}, ^{vs} vs. ^{vt}, ^{vt} vs. ^{vu}, ^{vu} vs. ^{vv}, ^{vv} vs. ^{vw}, ^{vw} vs. ^{vx}, ^{vx} vs. ^{vy}, ^{vy} vs. ^{vz}, ^{wa} vs. ^{wb}, ^{wb} vs. ^{wc}, ^{wc} vs. ^{wd}, ^{wd} vs. ^{we}, ^{we} vs. ^{wf}, ^{wf} vs. ^{wg}, ^{wg} vs. ^{wh}, ^{wh} vs. ^{wi}, ^{wi} vs. ^{wj}, ^{wj} vs. ^{wk}, ^{wk} vs. ^{wl}, ^{wl} vs. ^{wm}, ^{wm} vs. ^{wn}, ^{wn} vs. ^{wo}, ^{wo} vs. ^{wp}, ^{wp} vs. ^{wq}, ^{wq} vs. ^{wr}, ^{wr} vs. ^{ws}, ^{ws} vs. ^{wt}, ^{wt} vs. ^{wu}, ^{wu} vs. ^{wv}, ^{wv} vs. ^{ww}, ^{ww} vs. ^{wx}, ^{wx} vs. ^{wy}, ^{wy} vs. ^{wz}, ^{xa} vs. ^{xb}, ^{xb} vs. ^{xc}, ^{xc} vs. ^{xd}, ^{xd} vs. ^{xe}, ^{xe} vs. ^{xf}, ^{xf} vs. ^{xg}, ^{xg} vs. ^{xh}, ^{xh} vs. ^{xi}, ^{xi} vs. ^{xj}, ^{xj} vs. ^{xk}, ^{xk} vs. ^{xl}, ^{xl} vs. ^{xm}, ^{xm} vs. ^{xn}, ^{xn} vs. ^{xo}, ^{xo} vs. ^{xp}, ^{xp} vs. ^{xq}, ^{xq} vs. ^{xr}, ^{xr} vs. ^{xs}, ^{xs} vs. ^{xt}, ^{xt} vs. ^{xu}, ^{xu} vs. ^{xv}, ^{xv} vs. ^{xw}, ^{xw} vs. ^{xx}, ^{xx} vs. ^{xy}, ^{xy} vs. ^{xz}, ^{ya} vs. ^{yb}, ^{yb} vs. ^{yc}, ^{yc} vs. ^{yd}, ^{yd} vs. ^{ye}, ^{ye} vs. ^{yf}, ^{yf} vs. ^{yg}, ^{yg} vs. ^{yh}, ^{yh} vs. ^{yi}, ^{yi} vs. ^{yj}, ^{yj} vs. ^{yk}, ^{yk} vs. ^{yl}, ^{yl} vs. ^{ym}, ^{ym} vs. ^{yn}, ^{yn} vs. ^{yo}, ^{yo} vs. ^{yp}, ^{yp} vs. ^{yq}, ^{yq} vs. ^{yr}, ^{yr} vs. ^{ys}, ^{ys} vs. ^{yt}, ^{yt} vs. ^{yu}, ^{yu} vs. ^{yv}, ^{yv} vs. ^{yw}, ^{yw} vs. ^{yx}, ^{yx} vs. ^{yy}, ^{yy} vs. ^{yz}, ^{za} vs. ^{zb}, ^{zb} vs. ^{zc}, ^{zc} vs. ^{zd}, ^{zd} vs. ^{ze}, ^{ze} vs. ^{zf}, ^{zf} vs. ^{zg}, ^{zg} vs. ^{zh}, ^{zh} vs. ^{zi}, ^{zi} vs. ^{zj}, ^{zj} vs. ^{zk}, ^{zk} vs. ^{zl}, ^{zl} vs. ^{zm}, ^{zm} vs. ^{zn}, ^{zn} vs. ^{zo}, ^{zo} vs. ^{zp}, ^{zp} vs. ^{zq}, ^{zq} vs. ^{zr}, ^{zr} vs. ^{zs}, ^{zs} vs. ^{zt}, ^{zt} vs. ^{zu}, ^{zu} vs. ^{zv}, ^{zv} vs. ^{zw}, ^{zw} vs. ^{zx}, ^{zx} vs. ^{zy}, ^{zy} vs. ^{zz}, ^{aa} vs. ^{ab}, ^{ab} vs. ^{ac}, ^{ac} vs. ^{ad}, ^{ad} vs. ^{ae}, ^{ae} vs. ^{af}, ^{af} vs. ^{ag}, ^{ag} vs. ^{ah}, ^{ah} vs. ^{ai}, ^{ai} vs. ^{aj}, ^{aj} vs.

inverse, positive or no association between parity and BMD. However, when studies involving women with multi-parity were considered separately, they tended to show a more consistent inverse association between BMD and parity (Ozdemir *et al.* 2005; Sadat-Ali *et al.* 2005; El Maghraoui *et al.* 2007). Furthermore, association between parity and fracture has been inconsistent. While Fujiwara in 1997 (Fujiwara *et al.* 1997) found multi-parity (more than five children) to increase the risk of hip fracture, Henderson *et al.* (2000) found no such association. In contrast, Honkanen *et al.* (2000) reported a 29% reduction in distal forearm fracture risk associated with parity. Nulliparity was, however, consistently associated with high fracture risk (Petersen *et al.* 2002; Hillier *et al.* 2003). This is keeping with our observation of lower BMD and BMC among nulliparous women.

Inconsistent association between parity and BMD or fracture risk could be due to many reasons. Variables such as body proportions, breastfeeding practices, social habits menopausal status and nutrition, which vary between countries, could influence the associations. Similar to parity, studies on breastfeeding reported conflicting associations with BMD (Karlsson *et al.* 2001; Kojima *et al.* 2002; Ward *et al.* 2005). Cross-sectional design, used by most of these studies, would not allow the BMD changes associated with breastfeeding to be separated from that of pregnancy. Our data on breastfeeding were incomplete and did not allow us to separate the effects of pregnancy on BMD from that of breastfeeding.

Apart from BMD, parity may influence bone geometry. Repeated pregnancies could modify hip dimensions and indices of hip geometry which act as independent risk factors of hip fracture (El-Kaissi *et al.* 2005). Only few studies have examined changes in bone geometry associated with parity. Specker and Binkley found the femoral neck bone area to be 4% greater in women with more than seven children when compared with women with one to four children (Specker & Binkley 2005). In the same analysis, torsional bending strength, which includes structural and material bone properties, at the distal radius was greater with higher parity ($P = 0.01$). The greater femoral neck size and torsional bending strength in the distal radius may explain the reduced fracture risk

among women with high parity previously reported in some studies.

Pregnancy and lactation lead to increased bone turnover. Available data, however, do not indicate normal pregnancy to have a deleterious effect on maternal skeleton (Kaur *et al.* 2003; Ward *et al.* 2005). Repeated pregnancies, especially in countries where maternal nutrition is not emphasized, could lead to incomplete recovery of BMD at the end of each pregnancy leading to a net BMD loss which would contribute to low BMD in old age. Longitudinal changes in BMD during pregnancy and lactation should be monitored in Asian populations to see the effect of repeated pregnancies on maternal skeleton in countries where maternal nutrition can be suboptimal.

Lower BMD observed among nulliparous women could be related to low oestrogen levels. It can be argued that these women were nulliparous due to primary gonadal failure and had low exposure to oestrogen. We have no data to support this. Furthermore, nulliparous women do not get the benefit of renewal of skeleton with new bone material at the end of each pregnancy and lactation. Hence, they would carry a high risk of fracture.

Our study has a few limitations. Two provinces were not included in the study because of security reasons. These provinces have a majority of ethnic Tamils and Moors, but we were able to recruit them, roughly in the number that they represent in the population, from other provinces. Only the scanning centres were randomized but not the subjects. We had to include all the subjects gathered in scanning centres. This may have led to selection bias of subjects, limiting the external validity of results. We were unable to get a detailed history of period of breastfeeding or physical activity as it was not possible to do this in a community setting. Furthermore, only phalangeal BMD was measured and BMDs in other sites such as spine or hip in these subjects may have behaved in a different way.

In summary, we report higher phalangeal BMD and BMC associated with one to four pregnancies in this group of healthy, post-menopausal women selected from the community. Nulliparous and multi-parous women (more than four children) had lower phalangeal BMD and this would indicate their higher risk

of developing a fracture in old age. These BMD and BMC differences could be attributed to current age and weight difference between these groups. Even after adjusting for current age and weight, nulliparous women had the lowest phalangeal BMD indicating their vulnerability for fractures.

Acknowledgements

The authors acknowledge the support of Fonterra Lanka for providing the AccuDEXA scanner and funding for the study. Ms Anuradha Wickramasekare, a technician in the Center for Metabolic Bone diseases, helped maintain the central database.

This study was partly funded by the Fonterra Brands, Sri Lanka. They paid the salary of the technician and also provided the AccuDEXA machine for scanning. The authors worked completely on voluntary basis. They planned the study, supervised the data collection and analysed the data.

Conflict of interest

All authors declare that they have no competing interests.

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