

# Cardiovascular Disease Risk Factors in Thai Natural Menopause with First-Time Diagnosis of Low Bone Mass Density

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## ABSTRACT

**Objective:** To evaluate the prevalence of initial cardiovascular disease (CVD) risk factors in naturally postmenopausal Thai women with first-time diagnosis of low bone mass density (BMD), and compare with those reported among general Thai women of the same age range during the same studied time.

**Methods:** A retrospective cross-sectional study of initial CVD risk factors of 473 naturally postmenopausal Thai women (45-60 years) with the first-time diagnosis of osteopenia or osteoporosis without previous treatment for CVD risk factors, except for hypertension (HT) and diabetes mellitus (DM), was performed. Only subjects with all available initial CVD risk factors were recruited. Data included age, weight, height, waist circumference (WC), and underlying diseases. Extracted initial CVD risk factors were: HT, DM, body mass index (BMI), cholesterol level, triglyceride, high density lipoprotein, and family history of CVD. The main outcome was prevalence of initial CVD risk factors with 95% CI. Results were compared with data of previous Thai reports in women of the same age during the same time period.

**Results:** All subjects (86.3% osteopenic, 13.7% osteoporotic) had on average 3.6 years since menopause. Prevalence of women with initial CVD risk factors was 73.8%. The three most common risk factors were high BMI (48.6%), high WC (37.8%) and high cholesterol (22.2%). Only high BMI was more prevalent than previously reported. In contrast, the other factors were lower than previously published data.

**Conclusion:** With the exception of high BMI, initial CVD risk factors in this study were comparable to or lower than those reported in general Thai women of the same age during the same time period.

**Keywords:** CVD risk factors; low BMD; natural menopause; Thai (Siriraj Med J 2019;71: 189-195)

## INTRODUCTION

Osteopenia or osteoporosis is a condition that is characterized by low bone mineral density (BMD) and reduced bone strength increases risk of bone fractures. However, the overall prevalence of osteoporosis, the more severe condition, in postmenopausal Thai women was approximately 39%.<sup>1</sup> Many studies found cardiovascular disease (CVD) to be associated with osteoporosis.<sup>2</sup> Tanko, *et al.* reported that this increase in risk is proportional to the severity of osteoporosis at the time of diagnosis.<sup>3</sup> Thai women diagnosed with low BMD (osteopenia/osteoporosis)

are usually prescribed calcium supplementation because typical Thai diet is low in calcium. Calcium is also a key player in coagulation, and muscle and myocardial contraction. Thus, a change in calcium metabolism may participate in the development of CVD.<sup>4</sup>

Traditional CVD risk factors are categorized as either un-modifiable risk factors (e.g. age, gender) or modifiable risk factors [e.g. hypertension (HT), diabetes mellitus (DM), dyslipidemia (DLP), and obesity or overweight status]. With an increase in older population and the adoption of more and more Western lifestyle behaviors,

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Received 21 June 2018 Revised 26 September 2018 Accepted 5 March 2019

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<http://dx.doi.org/10.33192/Smj.2019.29>

Thailand is replacing its traditional high-carbohydrate diets, consisting largely of rice and vegetables, with a diet high in fat and sugar.<sup>5</sup> As a result, we can expect to see commensurate increases in the prevalence of CVD. The prevalence of several initial CVD risk factors has not been simultaneously studied in naturally postmenopausal Thai women with first time diagnosis of osteopenia/osteoporosis and crucially needed calcium supplementation.

Accordingly, the primary aim of this study was to investigate the prevalence of initial traditional CVD risk factors in naturally postmenopausal Thai women at the first-time diagnosis of osteopenia/osteoporosis. The secondary objective was to compare our findings with results from previous studies in Thai women in the same age range during the same time period.

## MATERIALS AND METHODS

This retrospective cross-sectional study was performed at the Gynecologic Endocrinology Unit, Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital. After the institutional ethical board approval (Si 276/2014) was obtained, data were collected from medical records between 1997 and 2014. Sample size calculation was ~500, which number included 10% for data loss by using the formula  $n = \frac{Z^2 \cdot P(1-P)}{d^2}$ . P was the prevalence of HT, which was one of the CVD risk factors ( $p=0.276$ ) from the latest studied Thai population in 2012.<sup>6</sup> Allowable error (d) was 0.0414 and relative error was 15%. The collected data were from the first participation in this unit. About 1,000 out-patient charts were reviewed and only 473 charts, as in Fig 1, were finally included when the following inclusion criteria were met: natural menopause, 45-60 years, the first-time diagnosis of osteopenia or osteoporosis without previous treatment. Patient charts with a history of metabolic bone disorders, drug affecting calcium and bone metabolism,

congenital or valvular heart disease, or cancer with bone metastasis were excluded. Reviewed data included age, weight, height, waist circumference (WC), and underlying diseases. CVD risk factors consisted of DM, HT, body mass index (BMI), cholesterol (Chol), triglyceride (TG), high density lipoprotein (HDL) and family history of CVD (female <65 years, male <55 years).

## Statistical analysis

PASW (SPSS) version 18 (SPSS Inc., Chicago, IL, USA.) was used. The results were reported as mean±SD, minimum, maximum and percentage with 95%CI. T-test was used to compare continuous variables eg. BMI, Wt, Ht, etc. Categorical data, eg. BMI ≥ 23 kg/m<sup>2</sup> etc. was analyzed by Pearson Chi-square test, and p-value <0.05 was statistically significant. The data were also compared with previously reported data of Thai population.

## RESULTS

473 patients with complete data were included in the final analysis. The mean age of patients was 53.5±4.1 years. All subjects were non-smoking with an average 3.6 years since menopause. Demographic data and clinical characteristics are shown in Table 1. Mean WC, Chol, TG, and HDL levels were all within normal ranges. Only mean high BMI for Asian women (≥ 23.0 kg/m<sup>2</sup>) in this study was higher than previously reported in Thai women. The overall prevalence of patients with traditional initial CVD risk factors was 73.8%. While approximately one-fourth of the subjects had no risk factor, 61 patients (12.9%) had 4-6 risk factors, and only one patient had all seven risk factors. The 3 most common risk factors were high BMI (48.6%), high WC (37.8%), and Chol ≥ 240 mg/dl (22.2%). The vast majority of women were osteopenic (408 patients, 86.3%), with only 65 (13.7%) women having osteoporosis (Fig 1).

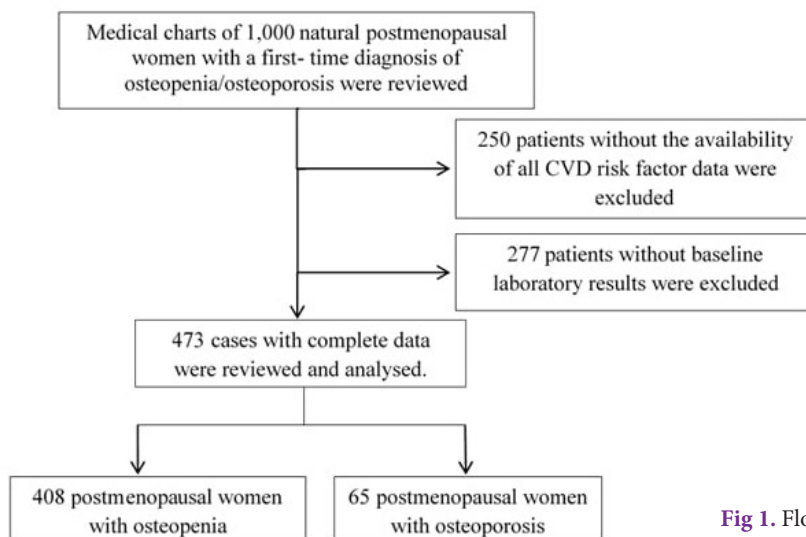


Fig 1. Flow diagram of subject selection process.

**TABLE 1.** Clinical characteristics, and prevalence and number of CVD risk factors, overall and by BMD group.

	All subjects (n = 473) Mean±SD	Osteopenia (n = 408) Mean±SD	Osteoporosis (n=65) Mean±SD	P-value*
Age (yrs)	53.5±4.1	53.4±4.0	53.7±4.1	0.595
Wt (kg)	55.7±8.7	56.0±8.6	53.8±8.5	0.066
Ht (cm)	154.7±5.2	154.8±5.1	154.3±5.7	0.501
BMI (kg/m <sup>2</sup> )	23.3±3.4	23.4±3.4	22.6±3.4	0.104
WC (cm)	78.1±8.3	78.3±8.3	76.6±8.1	0.113
Chol (mg/dl)	212.4±38.6	211.5±38.0	218.1±42.3	0.200
TG (mg/dl)	103.3±50.5	103.9±51.5	100.1±44.3	0.573
HDL (mg/dl)	65.5±15.9	64.6±16.0	67.5±15.4	0.177
<b>Number of risk factor, cases (%)</b>				
HT	67 (14.2%)	48 (11.8%)	19 (29.2%)	<0.001
DM	22 (4.7%)	17 (4.2%)	5 (7.7%)	0.210
BMI ≥ 23.0 (kg/m <sup>2</sup> )	230 (48.6%)	201 (49.3%)	29 (44.6%)	0.486
Chol ≥ 240 mg/dl	106 (22.2%)	85 (20.8%)	20 (30.8%)	0.073
TG ≥ 150 mg/dl	59 (12.5%)	53 (13%)	6 (9.2%)	0.394
HDL < 50 mg/dl	49 (10.4%)	46 (11.3%)	3 (4.6%)	0.102
WC > 80 cm	179 (37.8%)	159 (39%)	20 (30.8%)	0.205
Family history of CVD	94 (19.9%)	76 (18.6%)	18 (27.7%)	0.089
<b>Number of risk factors, cases (%)</b>				
0-1	237 (50.1%)	207 (50.8%)	30 (46.2%)	} 0.462
2-3	174 (36.8%)	149 (36.5%)	25 (38.4%)	
4-6	61 (12.9%)	51 (12.5%)	10 (15.4%)	
7	1 (0.2%)	1 (0.2%)	0 (0%)	

\*P-value &lt;0.05 indicates statistical significance

**Abbreviations:** BMD=bone mineral density, Wt=weight, Ht=height, BMI=body mass index, WC=waist circumference, Chol=cholesterol, TG=triglyceride, HDL=high density lipoprotein cholesterol, HT=hypertension, DM=diabetes mellitus, CVD=cardiovascular disease

Results of analysis between the osteopenia and osteoporosis subgroups are shown in [Table 1](#). Average age, anthropometric parameters, and baseline laboratory results were not significantly different between groups. HT, DM, high Chol and family history of CVD were higher in the osteoporosis group than in the osteopenia group. Of those, HT was the only risk factor that was statistically significantly higher in the osteoporosis group than in the osteopenia group ( $p < 0.001$ ). Also, prevalence of high BMI, high TG, low HDL and high WC were lower in the osteoporosis group, but without statistical significance. The number of cases with 0-1, 2-3, 4-6 and 7 CVD risk factors were comparable between groups.

The prevalence of each initial CVD risk factor with 95% CI, and the prevalence reported from other studies in Thai women conducted during the same period are shown in [Table 2](#). BMI  $\geq 23.0$  kg/m<sup>2</sup> was more prevalent in this study than in the 2010 report. HT, DM, high WC, high TG, and low HDL were also lower than in the previously published data. High Chol was also much lower than one previously published study, but the cut-off levels differed between the two studies (240 mg/dl vs 200 mg/dl, respectively). Family history of CVD was comparable with the 2006 report. Prevalence of DLP was also relatively high in this study, but without available previous data for comparison. Data from the National Health Examination Survey (NHES) V for the year 2015 was not available for comparison at the time that this manuscript was being prepared.

## DISCUSSION

This study set forth to investigate the prevalence of initial CVD risk factors in naturally postmenopausal Thai women with low BMD who crucially need calcium supplementation after the first-time diagnosis of osteopenia/osteoporosis at a large tertiary care hospital in Thailand. Only naturally postmenopausal women were studied, because surgically postmenopausal women would likely be younger and would likely not yet have developed low BMD. Moreover, low BMD is not always identifiable soon after oophorectomy in younger women. Given that the average age of subjects was in the early naturally postmenopausal period, osteopenia was found to be more prevalent than osteoporosis. Interestingly, 26% of the subjects at the average age of 53.5 years still did not have any identifiable traditional CVD risk factors, and one-fourth of the cases had only one factor. However, half of the patients in this study had  $\geq 2$  risk factors and 12.5% had  $\geq 4$  risk factors.

The cross-sectional data from the NHES III in 2004, revealed a prevalence of overweight and obesity of 4.0%

in a sample of Thai adults aged 35-59 years.<sup>7</sup> In another report, Thai women aged 46-55 years had the highest risk of being overweight or obese, and this may be due to the weight gain during important life transition events like retirement and menopause.<sup>8</sup> In a study conducted in Bangkok at another tertiary-care hospital, risk factors of hypercholesterolemia increased among Thai women: advanced age (OR:3.19), and family history of DLP (OR:1.59). It also reported that total Chol and TG were strongly associated with age, BMI and family history of DLP, while HDL was inversely associated with BMI.<sup>9</sup> In that study, women aged 40-59 years had an OR of 1.77 (95%CI: 1.27-1.48) of developing hypercholesterolemia compared to women aged  $< 40$  years. However, a positive association between increasing age and BMI and total Chol, TG and total Chol/HDL ratio were also noted. Undoubtedly, overweight and obese women had higher TG ( $p < 0.001$ ). A study in Taiwan by Tsai WL., also found that the risk of hypercholesterolemia increased with increasing BMI in both genders.<sup>10</sup> In addition, women with a family history of DLP had a mean total Chol higher than those without a family history of DLP ( $p < 0.001$ ). In a study from Japan, Kawada T. observed that odd ratios for hypercholesterolemia ( $\geq 240$  mg/dl) also increased across higher BMI quartiles (OR:1.0-4.6).<sup>11</sup>

The average baseline characteristics of the patients in this study were mostly within normal ranges and approximately one fourth of the women had no initial CVD risk factors. Regarding HT and DM in Thailand, the age-specific prevalence of individuals having one or both conditions increased as age increased and peaked at later age,  $\geq 80$  years. Prevalence of coexisting HI and DM was reported to be highest in the 60-69 years' age group.<sup>6</sup> Total prevalence of DM was higher in urban residents than in rural residents for both men and women ( $p < 0.001$ ).<sup>7</sup> However, the proportions of DM cases with HT did not significantly decrease for either gender.

This study revealed some other interesting outcomes. Firstly, the prevalence of high BMI, high Chol, and family history of CVD, were comparable with the results of other Thai studies in patients of comparable ages. In Thailand, a significant increase in the prevalence of overweight and obesity was observed, from 1991 (25%) to 2004 (48%) among Thai adults aged 35-59 years.<sup>13</sup> Also, from 2004 to 2009, the proportion of women with DM and abdominal obesity increased 18% and the proportion of women who had DM and high Chol increased 23.5%.<sup>14</sup> The increase in BMI and prevalence of obesity in Thailand were reported to be consistent with rates of increase in other Asian countries.<sup>15</sup> It is known that the risk of developing CVD increases twofold after

**TABLE 2.** Prevalence of each CVD risk factor compared with previous Thai reports.

CVD risk factors	Prevalence (%)	95%CI	The other National Thai studies	
			Population	Prevalence (%)
HT	14.2	11.3-17.6	Thai women aged 45-59 years Central, Northern, North, South Survey (urban/rural area) NHES III <sup>7</sup>	34.6
DM	4.7	3.1-6.9	Thai women aged 45-59 years Central, Northern, North, South Survey (urban/rural area) NHES III <sup>7</sup>	12.8
BMI $\geq 23$ kg/m <sup>2</sup>	48.6	44.2-53.1	3,275 women, average age 40.8 $\pm 16.6$ years (women aged 36-45, 46-55, 56-65 with OR for overweight 2.5 (1.6-3.9), 4.8 (3.0-7.6), 2.9 (1.8-4.8) respectively, $p < 0.001$ ) Nationally representative sample covering all geographic regions of Thailand <sup>8</sup>	44.9
DLP	44.4	40-48.9		NA
Cholesterol $\geq 240$ mg/dl	22.2	18.7-26.2	510 women aged 40-59 who participated in annual health examination at a tertiary-care hospital, Bangkok (cholesterol $\geq 200$ mg/dl) <sup>9</sup>	71.9
TG $\geq 150$ mg/dl	12.5	9.8-15.8	Thai women aged 40-59 years Sampling by province, region, district, village, the sex and agespecific group. NHES IV <sup>12</sup>	40-49 years: 29.6% 50-59 years: 42.9%
HDL $> 50$ mg/dl	10.4	7.9-13.4	Thai women aged 40-59 years Sampling by province, region, district, village, the sex and agespecific group. NHES IV <sup>10</sup>	40-49 years: 56.4% 50-59 years: 58.4%
WC $> 80$ cm	37.8	33.6-42.3	Thai women aged 40-59 years Sampling by province, region, district, village, the sex and age- specific group. NHES IV <sup>12</sup>	40-49 years: 51.0% 50-59 years: 57.6%
Family history of CVD	19.9	16.5-23.7	851 women with known family history of CVD who participated in annual health examination at a tertiary-care hospital, Bangkok <sup>9</sup>	19.8

**Abbreviations:** CVD=cardiovascular disease; CI=confidence interval; HT=hypertension; NHES=National Health Examination Survey; DM=diabetes mellitus; BMI=body mass index; OR=odds ratio; DLP=dyslipidemia; NA=not available; Chol=cholesterol; TG=triglycerides; HDL=high density lipoprotein cholesterol; WC=waist circumference

Thai NHES III= 2004 (Multistage, probability sampling of Thai population aged  $\geq 15$  years) Thai NHES IV = 2009 (Multistage, stratified sampling of Thai population aged  $\geq 20$  years) Thai NHES V = 2015 (Published data not available at the time this manuscript was drafted)

menopause. Decreased estrogen level may be associated with CVD risk.<sup>16,17</sup> Prevalence of family history of CVD in this study was similar to the other Thai study conducted during the same time period to which we compare our results. This may explain why subjects in both studies were homogenous Thai Indochina population.

Secondly, the prevalence of HT, high WC, high TG and low HDL were much lower in this study than in the other studies to which each was compared. This may be explained by the reason that the women in this study were early naturally postmenopausal women who had received the first-time diagnosis of osteopenia/osteoporosis. This interesting finding should be studied more extensively. Many studies reported that postmenopausal women have increased total Chol, increased LDL, increased TG, increased lipoprotein (a), and decreased HDL. The change in lipid profile may also be partly attributed to increased abdominal adiposity in menopausal women.<sup>16</sup> Unfortunately, prevalence of DLP from previous study was not available for comparison in this report.

Menopause causes a significant increase in total peripheral resistance and loss of arterial vasodilatation. This may contribute to increases in BP.<sup>10</sup> Differences in the prevalence in this study and the comparative studies shown in Table 2 could also be differences in study design. The population in this study was derived from a single-center, tertiary care hospital. The proportions of subjects with numbers of CVD risk factors (i.e. 0-1, 2-3, 4-6 and 7) were not significantly different between the two groups. However, the prevalence of HT in the osteoporosis group was significantly higher than the osteopenia group ( $p < 0.001$ ). This difference may be explained by the older mean age of patients in the osteoporosis group ( $p > 0.05$ ).

Family history of CVD is an un-modifiable risk factor, and other modifiable risk factors, such as HT and DM might increase in prevalence as women age. The prevalence of HT reported from the NHES III study in 2004 and reported in 2008 among Thai women increased from 34.6% (45-59 yr), to 48.1% (60-69 yr) and 54.1% (70-79 yr). Also, the prevalence of DM in that study increased from 12.8% (45-59 yr), to 19.1% (60-69 yr) and 16.1% (70-79yr).<sup>18</sup> The cross-sectional data from the NHES IV reported in 2009 showed that high WC also increased as Thai women aged, from 51.0% (40-49 yr) to 57.6% (50-59yr). Result from the same report in 2009 showed, TG  $\geq 150$  mg/dl also increased with age, from 29.6% (40-49 yr) to 42.9% (50-59 yr), while HDL  $< 50$  mg/dl showed only a slight increase in prevalence from 56.4% (40-49 yr) to 58.4% (50-59 yr). Results from the National Thai Food Consumption Survey in 2010 of other samples covering all geographic regions of Thailand,

showed that women aged 46-55 year had the highest OR for BMI  $\geq 23.0$  kg/m<sup>2</sup> compared to women aged  $< 45$  years and 56-65 years (OR:2.5 vs 2.9, respectively). The results from previous Thai reports imply that as Thai women age, they may have more traditional CVD risk factors.

This study showed that naturally postmenopausal Thai women with osteopenia/osteoporosis had initially comparable or lower CVD risks than Thai women in the general population of the same ages during the same study time frame. However, the CVD risk factors were different among the osteopenia and osteoporosis groups and need future study.

This study has some mentionable limitations. First and consistent with the retrospective nature of this study, some patient data may have been missing or incomplete which they were excluded from the final analysis. Second, the patients we studied were hospital-based, from a single center referred with mainly menopausal symptom complaints. Behavioral and lifestyle characteristics such as alcohol consumption, and exercise habits should also be collected for analysis.

## CONCLUSION

Prevalence of initial CVD risk factors in this study was 73.8%. With the exception of high BMI, initial CVD risk factors in this study subjects were comparable to or lower than those found in Thai women in the general population of the same age during the same time period.

## ACKNOWLEDGMENTS

The authors gratefully acknowledge Mr. Suttipol Udompunturak, a statistician, for assistance with statistical analyses.

**Conflict of Interest:** The authors report no funding sources in this work and declare no conflict of interest.

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