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Dyslipidemia in Post-menopausal Women of Western Nepal: A Community-Based Comparative Study

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ABSTRACT

INTRODUCTION: Dyslipidemia is a modifiable risk factor for cardiovascular diseases (CVDs). Menopause-related hormonal alterations are responsible for dyslipidemia. Early identification of such risk factors aids in the prevention and prompt management of CVDs. The current study was done to evaluate the prevalence of dyslipidemia in post-menopausal women and compare the lipid profiles between pre-menopausal and post-menopausal women. **MATERIALS AND METHODS:** This community-based comparative cross-sectional study was conducted among the female population of the Siyari rural community, Rupandehi from January 2022 to April 2022. After obtaining verbal and written consent, a total of 322 fasting samples were collected from healthy women based on the questionnaire strategy. Among them 160 were pre-menopausal and 162 were post-menopausal. Serum lipids for Total Cholesterol (TC), Triglycerides (TG), and High Density Lipoprotein (HDL) were estimated by automated Humalyzer 600. Low Density Lipoprotein (LDL), Very Low Density Lipoprotein (VLDL), and lipid ratios were calculated. **RESULTS:** The prevalence of dyslipidemia was high among post-menopausal women (73.5%). TG, TC, VLDL, LDL, TC/HDL, TG/HDL, and LDL/HDL were significantly increased in post-menopausal women compared to pre-menopausal women ($p < 0.001$), whereas serum HDL was significantly decreased ($p = 0.032$). **CONCLUSIONS:** Higher serum lipids and lipid ratios in post-menopausal women could lead to increased CVD risks and other related complications in the long term.

Keywords: Cardiovascular disease, Dyslipidemia, Lipid profile, Pre-menopause, Post-menopause

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INTRODUCTION

Menopause is defined as the permanent cessation of menstruation resulting from loss of ovarian follicular activity for at least one year [1]. The average age of menopause for Nepalese women is 48.7 years [2]. Females after menopause undergo several metabolic alterations, particularly due to a decline in estrogen levels, increasing the risk for cardiovascular diseases (CVDs) [3,4]. The third report of the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP III) criteria, defines dyslipidemia with the following cut-off values: hypercholesterolemia - serum total cholesterol (TC) level ≥ 200mg/dl; hypertriglyceridemia - serum triglycerides (TG) level ≥ 150 mg/dl; low high-density lipoprotein cholesterol (HDL-C) – HDL-C level ≤ 40 mg/dl for both men and women; high low-density lipoprotein cholesterol (LDL-C) – LDL-C level ≥ 100 mg/dl [5]. Dyslipidemia, exacerbated by menopausal transition, is a modifiable risk factor for CVDs [6]. After menopause, women experience serum lipid changes owing to a significant decrease in the sex hormone estrogen. Their LDL-C, TC, and TG increase and HDL-C decreases [7]. These alterations in lipid metabolism are thought to be a substantial component of CVD risk [8]. There are also direct effects of estrogen deficiency on body fat distribution, insulin action, the arterial wall, and

fibrinolysis that may influence CVD risk [9]. Therefore, it necessitates screening of every woman undergoing menopause for early diagnosis and prevention of CVDs. Various studies have compared lipid profiles of pre-and post-menopausal women [10-15]. However, studies from Nepal, especially the Western community of Nepal are rare. In this context, we aimed to evaluate the prevalence of dyslipidemia in post-menopausal women as well as to compare the lipid profiles between pre-and post-menopausal women from a local community of Western Nepal.

MATERIALS AND METHODS

Study design and setting

This community-based comparative, cross-sectional study was conducted from January 2022 to April 2022 for four months in Siyari rural municipality, Rupandehi, Province No.5, Nepal.

Participants, sample size and sampling technique

A total of 322 participants using purposive sampling technique, were included in the study, where 160 were pre-menopausal and 162 were post-menopausal women. The pre-menopausal women between the ages of 25 and 50 years and post-menopausal women > 45 years with at least one year of menopause were included in the study. Pregnant and lactating pre-menopausal women, women who had undergone menopause due to hysterectomy or cessation of periods other than by a natural cause, women having comorbidities like diabetes mellitus, hypertension, heart disease, and women under drugs that affect serum lipid profile like statins and fibrates were excluded from the study.

Data collection procedure and study variables

A study proforma was filled out via a face-to-face interview with the participants at their homes. Weight and height were measured by a weighing machine and measuring tape respectively. BMI was calculated as (body weight in kg) / (height in metre^2). Waist circumference (WC) was measured by a measuring tape in a horizontal plane around the abdomen at the level of the iliac crest. Blood pressure (BP) was measured by Sphygmomanometer after resting for 5 minutes. The participants were advised to fast for 10 to 12 hours in order to obtain blood samples for lipid profiles. On the next day around 7:00 AM to 9:00 AM, following the standard aseptic technique, 5 ml of fasting blood sample was collected in plain vials. The samples were kept in an ice-pack containing box for transportation and were processed in the central laboratory of Universal College of Medical Sciences and Teaching Hospital (UCMS). The serum was separated by centrifugation at 3000 rpm for 10 minutes. Serum lipids (TG, TC, and HDL) were estimated by using Glycerol Phosphate Oxidase - Phenol 4-aminoantipyrine Peroxidase (GPO-PAP) method, Cholesterol Oxidase-Phenol 4-aminoantipyrine Peroxidase (CHOD-PAP) method and Direct select inhibitory method respectively by an automated analyzer (Humalyzer 600, Germany) whereas VLDL was calculated by using the formula; VLDL = TG/5 and LDL by using Friedewald's equation; LDL = TC - (VLDL + HDL). Different lipid ratios like TC/HDL, TG/HDL, and LDL/HDL were also calculated. Dyslipidemia was defined according to the NCEP ATP III criteria [5].

Statistical analysis and data management

The data were entered in Microsoft Excel and analyzed by Statistical Package for Social Sciences (SPSS version 20). The qualitative data were expressed as frequency and percentage. The Shapiro-Wilk test was performed to evaluate the normality of the quantitative variables. Since the data were non-normal, non-parametric tests were employed to analyze and were expressed in their median and interquartile range. Odds ratio, Mann-Whitney U Test, and Spearman correlation were performed for analysis. A p-value of < 0.05 was considered statistically significant.

Ethical considerations

Ethical approval was obtained from the institutional review committee of Universal College of Medical Sciences and Teaching Hospital, Bhairahawa (IRC no: UCMS/IRC/003/22). Both verbal and written consent was taken from the participants before the study.

RESULTS

A total of 322 female participants were included in this study, of which 160 (49.69%) were pre- menopausal and 162 (50.31%) were post-menopausal (Figure 1). Participants between the ages of 25 to 93 years were included in the study. The median age of pre-menopausal and postmenopausal women were 35 (30 - 40) years and 60 (55- 67) years respectively. The prevalence of dyslipidemia among the study population was 65.2% (n = 210). Figure 2 shows the distribution of dyslipidemia in study groups. Post-menopausal women had significantly higher odds of having dyslipidemia compared to premenopausal women (OR =2.09; p = 0.002) as shown in Table 1.

Table 2 shows the distribution of clinical variables (BMI, WC, and blood pressure) and serum lipid profile

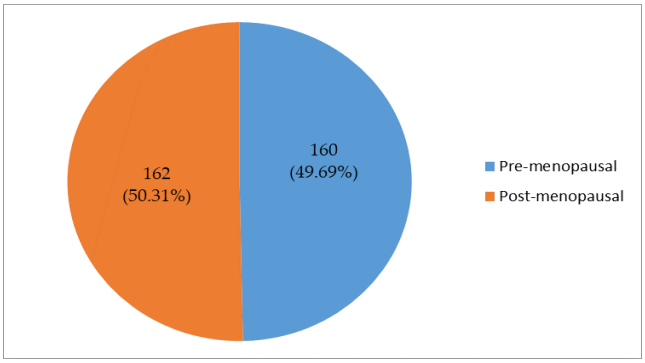

Figure 1|Distribution of study participants based on menopausal status.

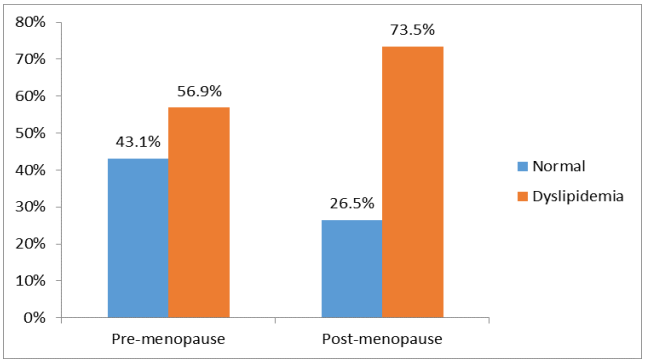

Figure 2|Dyslipidemia in pre-menopausal and post-menopausal women

between pre-menopausal and post-menopausal women. The post-menopausal group had significantly higher waist circumference, systolic and diastolic blood pressure compared to the pre-menopausal group. All of the serum lipid parameters significantly differed between the study groups. Their median levels, except HDL level and including the lipid ratios, were higher in the post-menopausal participants. The median serum HDL levels were significantly lower among post-menopausal women compared to pre-menopausal women. Serum TG, TC, LDL, and VLDL were positively correlated with age, WC, and BMI whereas serum HDL was negatively correlated with the age of participants (Table 3).

Table 1|Dyslipidemia in post-menopausal and pre-menopausal women along with odds ratio

Study Groups	Dyslipidemia		Odds of dyslipidemia	Odds Ratio (OR)	P-value	95% CI of OR
	Yes	No				
Post-menopausal	119	43	2.76	2.09	**0.002**	1.31 to 3.35
Pre-menopausal	91	69	1.32			

Table 2|Clinical variables and serum lipid profile of the study population

Variables	Total population (n=322)	Pre-menopause (n=160)	Post-menopause (n=162)	p-value
BMI (kg/m²)	25.4 (23.0 -28.3)	25.2 (22.9-28.1)	25.9 (23.0-29.2)	0.433
WC (cm)	91.4 (83.8-99.1)	86.4 (81.3-96.5)	93.9 (83.8-101.6)	**0.001**
SBP (mm Hg)	120.0 (113.7-130.0)	120.0 (110.0 - 120.0)	130.0 (120.0-140.0)	**<0.001**
DBP (mm Hg)	80.0 (80.0-90.0)	80.0 (80.0-82.0)	80.0 (80.0-90.0)	**<0.001**
TG (mg/dl)	120.0 (91.5-160.0)	110.0 (82.0-150.0)	129.5 (109.7- 170.0)	**<0.001**
TC (mg/dl)	166.0 (142.0-200.0)	157.0 (128.0-191.5)	178.0 (150.0-205.7)	**<0.001**
HDL (mg/dl)	48.0 (41.0-58.0)	48.0 (42.0-58.0)	46.0 (39.7-56.0)	**0.032**
VLDL (mg/dl)	24.0 (18.3-32.0)	22.0 (16.4-30.0)	25.9 (21.9-34.0)	**<0.001**
LDL (mg/dl)	92.9 (66.0-121.0)	79.7 (60.7-113.3)	101.7 (76.6-128.5)	**<0.001**
TC/HDL	3.4 (2.7-4.2)	3.2 (2.4-3.9)	3.7 (3.0-4.5)	**<0.001**
TG/HDL	2.5 (1.8-3.3)	2.1(1.6-3.0)	2.7 (2.0-3.7)	**<0.001**
LDL/HDL	1.9 (1.3-2.5)	1.6 (1.1-2.4)	2.1 (1.6-2.8)	**<0.001**

***Abbreviations*:** Body Mass Index(BMI), Waist Circumference (WC), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Triglyceride (TG), Total Cholesterol (TC), High Density Lipoprotein (HDL), Very Low Density Lipoprotein (VLDL), Low Density Lipoprotein (LDL) . Data expressed in Median value with 25th and 75th percentile included. p-values obtained from Mann Whitney U test. $p < 0.05$ considered statistically significant.

Table 3| Correlation of serum lipids with socio-demographic and clinical parameters

Serum lipids	Age		WC		BMI		SBP		DBP	
	ϱ	p-value	ϱ	p-value	ϱ	p- value	ϱ	p-value	ϱ	p-value
TG (mg/dl)	0.232	**<0.001**	0.204	**<0.001**	0.158	**0.005**	0.092	0.100	0.119	**0.033**
TC (mg/dl)	0.179	**0.001**	0.201	**<0.001**	0.201	**<0.001**	0.186	**0.001**	0.103	0.065
HDL(mg/dl)	-0.132	**0.018**	-0.025	0.651	0.025	0.655	-0.083	0.139	-0.083	0.138
VLDL(mg/dl)	0.232	**<0.001**	0.204	**<0.001**	0.158	**0.005**	0.092	0.100	0.119	**0.033**
LDL(mg/dl)	0.162	**0.004**	0.170	**0.002**	0.166	**0.003**	0.183	**0.001**	0.096	0.086

Abbreviations: Body Mass Index(BMI), Waist Circumference (WC), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Triglyceride (TG), Total Cholesterol (TC), High Density Lipoprotein (HDL), Very Low Density Lipoprotein (VLDL), Low Density Lipoprotein (LDL) , Correlation coefficient (ϱ). p-values obtained from Spearman's Correlation Analysis. $p < 0.05$ considered statistically significant.

DISCUSSION

Menopause is a special condition of estrogen deficiency that presents with several metabolic alterations [3]. In our study, post-menopausal women had a significantly higher prevalence of dyslipidemia than premenopausal women (OR = 2.09). There have been limited studies from Nepal regarding the prevalence of dyslipidemia among post-menopausal women. A study from Cameroon showed a high prevalence of dyslipidemia at 61%, especially among females recently entering menopause [16]. Another study from Beijing also reported a high prevalence of dyslipidemia (69.7%) in postmenopausal women [17]. Serum TG, TC, VLDL, LDL, TG/HDL, TC/HDL, and LDL//HDL were significantly higher in post-menopausal women than pre-menopausal group except for serum HDL, which was significantly lower.

In agreement with our results, various studies have reported increased serum TG, TC, VLDL, LDL, and decreased HDL among post-menopausal women [10-13]. Shenoy R et al. found no difference in HDL concentrations between the groups, with other parameters still being significantly higher in post-menopausal women [14]. However, Pardhe BD et al. showed increased HDL concentrations in post-menopausal women [15]. The alteration in serum lipids is thought to be due to a deficiency of estrogen in post-menopausal women. Estrogen has various effects on lipid metabolism [18]. It increases lipoprotein lipase activity, reducing serum triglyceride; increases the hepatic synthesis of LDL receptors resulting in increased uptake of LDL, and decreases circulating LDL levels. It also increases HDL levels by decreasing hepatic lipase activity. Decreases in estrogen concentrations after menopause tend to reverse these processes [4]. The cardio-protective effects of estrogen can be explained through its multiple actions and are especially appreciable during its deficiency. The decrease in estrogen levels in post-menopausal women is associated with the loss of subcutaneous fat and an increase in abdominal fat [19]. These lipid changes are also attributed to an increase in abdominal adiposity, especially visceral adiposity occurring during the menopausal transition. A higher amount of free fatty acids (FFA) produced by the visceral adipose tissue contributes to increased secretion of apolipoprotein B (apo B) - containing particles in the liver. This finally leads to increased production of VLDL and triglycerides. Increases in FFA also activate hepatic lipase with a predominance of atherogenic, small dense LDL particles, and a reduction in large anti-atherogenic HDL_2 particles [7].

Various studies have reported diverse results regarding serum HDL levels in post-menopausal women. This difference may be attributed to the alterations in sub-fractions of HDL. Estrogen deficiency after menopause raises HDL_3 cholesterol and lowers HDL_2 fraction [20]. Thus, measurement of HDL cholesterol alone may disguise the important changes occurring in the HDL sub-fractions. It seems likely that the fall in HDL cholesterol with the menopause reported in our study was due to a fall in the HDL_2 sub-fraction. The present study showed elevated TC/HDL, TG/HDL, and LDL/ HDL ratios in post-menopausal women suggestive of increased CVD risk. Similar findings are observed in other studies as well [10-12,14,15]. The Framingham study [21] reported that persons with LDL/HDL ratio greater than five are at higher risk of developing CVD, and persons with LDL/HDL ratio between 2 and 5 are at intermediate risk. In our study, the LDL/HDL ratio was 2.1 (1.6-2.8) in post-menopausal women which suggest an intermediate risk of developing CVD. In

contrast, LDL/HDL in the pre-menopausal women was significantly lower at 1.6, suggesting lower CVD risk, despite prevailing dyslipidemia in this group as well.

In this study, WC, SBP, and DBP were also significantly higher in post-menopausal women. This is in accordance with other published reports [10,13]. The decrease in estrogen levels in post-menopausal women is associated with the loss of subcutaneous fat and an increase in abdominal fat [19] leading to increase in waist circumference. High blood pressure in estrogen deficiency may be due to increased thromboxane A_2 release and endothelin production causing vasoconstriction [22]. We did not include the measurement of various sub-fractions of HDL, which could have provided better explanations regarding CVD risk in post-menopausal women. Larger studies with the inclusion of related co-morbidities and CVD risk factors would certainly give better insight and are highly recommended. Furthermore, longitudinal studies assessing whether such risks really translate to CVDs are also required.

CONCLUSIONS

Alteration in lipid profile and higher prevalence of dyslipidemia in postmenopausal women indicate an elevated risk of cardiovascular disease. Prevention through changes in lifestyle, or early detection and treatment of dyslipidemia is recommended for the prevention of cardiovascular diseases in Nepalese women reaching menopause.

ADDITIONAL INFORMATION AND DECLARATIONS

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Data Availability: Data will be available upon request to corresponding authors after valid reason.

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