

## Effect of Menopause on Low Density Lipoprotein

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### ABSTRACT

**Background and Objectives:** The present study was done on postmenopausal and premenopausal women with an objective to evaluate the effect of menopause on LDL cholesterol.

**Patients & methods:** This cross-sectional analytical study was done in the Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital, Dhaka over a period of 1 year between July 2012 to June 2013. A total of 60 women who underwent natural menopause were consecutively included in the study as case, while an equal number of premenopausal women were included as control. The outcome variable was level of serum LDL cholesterol.

**Result:** The study demonstrated that 60% of postmenopausal women were > 50 years old with mean age being  $51.2 \pm 2.7$  years, whereas 40% of premenopausal women were in their 4<sup>th</sup> decades life with mean age being  $39.1 \pm 8.1$  years ( $p = 0.001$ ). There was no significant difference between the groups in terms of BMI with mean BMI of the former and the later groups being  $24.45 \pm 3.43$  and  $23.76 \pm 3.46$  kg/m<sup>2</sup>. The mean serum cholesterol was observed to be significantly higher in case group than that in the control group ( $212.3 \pm 50.1$  vs.  $186.3 \pm 38.2$  mg/dl,  $p = 0.002$ ). The LDL cholesterol was also significantly higher in the case group than that in the control group ( $141.47 \pm 47.9$  vs.  $124.2 \pm 31.5$  mg/dl,  $p < 0.001$ ). However, the groups were almost homogeneous with respect to HDL cholesterol and triglycerides ( $38.2 \pm 5.0$  vs.  $37.6 \pm 5.3$  mg/dl,  $p = 0.526$  and  $167.0 \pm 67.2$  vs.  $181.0 \pm 82.6$  mg/dl,  $p = 0.311$  respectively). Nearly three-quarters (73.3%) of the cases exhibited elevated serum LDL cholesterol compared to one-third (33.3%) of the controls. The risk of having raised LDL in cases is more than 5(95% CI = 2.5 - 12.1) times higher than that in controls. The correlation graph between duration of menopause and serum LDL level showed that the two variables bear linear relationship ( $r = +0.338$ ,  $p = 0.008$ ).

**Conclusion:** The postmenopausal women are at increased risk of having higher LDL cholesterol than the premenopausal women and longer the duration of menopause the higher the level of LDL Cholesterol.

**Key words:** Menopause, Postmenopausal, Low-Density Lipoprotein (LDL).

### INTRODUCTION

The word menopause literally means the end of monthly cycles from the Greek word pausis (cessation) and the root men (month).<sup>1</sup> By definition permanent cessation of menstruation is called menopause. But it is not just the cessation of menstruation but also depletion of ovarian

follicles leading to decrease in ovarian hormones<sup>2</sup> which continue long after final menstrual period.<sup>2</sup> Premenopausal women are said to be protected against coronary heart disease (CHD), but this protection is lost once the women become postmenopausal. Oestrogens have a favourable effect on lipid profile; they lower LDL-C and elevate

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HDL-C.<sup>3</sup> Oestrogens are thought to increase HDL cholesterol by reducing hepatic triglycerides lipase activity that catabolizes HDL.<sup>4,5</sup> Menopause is an oestrogen deficient state. After menopause the incidence of CHD rises to approach that for men of similar age. This is most probably due to oestrogen deficiency because in young woman where oestrogen production is high and serum lipids are normal.<sup>6</sup>

Coronary Artery Disease is the leading cause of death among the postmenopausal women and this is due to estrogen deficiency. As estrogen deficiency causes rise of LDL and decrease of HDL leading to faster atherosclerosis which explains the increased incidence of coronary heart disease in postmenopausal women. Many of these women die from the disease and those who survive suffer from disability. Although certain form of CAD can be treated medically or surgically, the most effective means to decrease the impact of CHD on women's health is by modifying the contribution of specific factors that increase the risk of the disease. So screening the postmenopausal women for lipid profile will go a long way to prevent the disease or its consequences by averting the altered state of lipid profile as far as possible. That purpose the present study was intended to determine the level of LDL cholesterol of postmenopausal women.

## PATIENTS & METHODS:

This cross-sectional analytical study was carried out in the Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital, Dhaka over a period of 1 year from July 2012 to June 2013. A total of 60 women (ranging from 46-55 years) who underwent natural menopause were consecutively included in the study as case, while an equal number of premenopausal women with age close to those of cases (36 - 45 years) were included as control. However, cases of

surgical and premature menopause (menopause below 30 years) were excluded from the study. Besides, subjects with cardiovascular disease, diabetes mellitus, hypothyroids, hypertension, familial hypertriglyceridemia, postmenopausal bleeding, long term steroid therapy, oophorectomy, those on exogenous hormone or hormone replacement therapy, intake of lipid lowering drugs or any surgery were excluded from the study. The main outcome variable was level of serum LDL cholesterol. Five ml of venous blood was collected from each subject after an overnight fast of 12-14 hours. Serum was separated within one hour of blood collection and was then stored at 20 degree Celcius until analyzed for LDL cholesterol.<sup>7</sup> The LDL cholesterol was estimated by using Friedewald's<sup>8</sup> formula as:  $LDL\ cholesterol = Total\ cholesterol - (1/5\ TG + HDL\ Cholesterol)$ . Data were analysed using SPSS (Statistical Package for Social Sciences), version 17. The test statistics used to analyse the data were Chi-square ( $\chi^2$ ) Test, Unpaired t-Test and Pearsons correlation with level of significance being set at 5%.

## RESULTS

### **Demographic and anthropometric characteristics:**

The mean ages of the cases and control were  $51.2 \pm 2.7$  and  $39.1 \pm 8.1$  years respectively ( $p = <0.001$ ). There was no significant difference between the groups in terms of BMI with mean BMI of the former and the later groups being  $24.45 \pm 3.43$  and  $23.76 \pm 3.46$  kg/m<sup>2</sup> respectively (Table I).

### **Comparison of lipid profile between groups:**

The mean serum cholesterol was observed to be significantly higher in case group than that in the control group ( $212.3 \pm 50.1$  vs.  $186.3 \pm 38.2$  mg/dl,  $p = 0.002$ ). The LDL cholesterol was also significantly higher in the case group than that in the control group ( $141.47 \pm 47.9$  vs.  $124.2 \pm 31.5$

mg/dl,  $p < 0.001$ ). However, the groups were almost homogeneous with respect to HDL cholesterol and triglycerides ( $38.2 \pm 5.0$  vs.  $37.6 \pm 5.3$  mg/dl,  $p = 0.526$  and  $167.0 \pm 67.2$  vs.  $181.0 \pm 82.63$  mg/dl,  $p = 0.311$  respectively) (Table II).

**TABLE I. Demographic characteristics of case and control groups**

Demography	Group		p-value
	Case (n = 60)	Control (n = 60)	
<b>Age (yrs)<sup>#</sup></b>			
36-40	0(0.0)	34(40.0)	
41-45	0(0.0)	26(60.0)	
46-50	24 (40.0)	0(0.0)	
51-55	36 (60.0)	(0.0)	
Mean $\pm$ SD	51.2 $\pm$ 2.7	39.1 $\pm$ 8.1	< 0.001
<b>BMI<sup>#</sup> (kg/m<sup>2</sup>)</b>	24.45 $\pm$ 3.43	23.76 $\pm$ 3.46	0.279

Figures in the parentheses indicate corresponding %;

<sup>#</sup>Data were analyzed using Unpaired t-Test and were presented as mean  $\pm$  SD.

**TABLE II. Comparison of lipid profile between case and control groups (n = 338)**

Lipid profile(mg/dl)	Group		p-value
	Case (n = 60)	Control (n = 60)	
Total cholesterol	212.3 $\pm$ 50.1	186.3 $\pm$ 38.2	0.002
LDL cholesterol	141.47 $\pm$ 47.9	124.2 $\pm$ 31.5	<0.001
HDL cholesterol	38.2 $\pm$ 5.0	37.6 $\pm$ 5.3	0.526
Triglycerides	167.0 $\pm$ 67.2	181.0 $\pm$ 82.63	0.311

<sup>#</sup>Data were analyzed using Unpaired t-Test and were presented as mean  $\pm$  SD.

#### Distribution of LDL level among the study subjects:

Nearly three-quarters (73.3%) of the cases exhibited elevated serum LDL cholesterol compared to one-third (33.3%) of the controls. The risk of having raised LDL in cases is more than 5(95% CI = 2.5 - 12.1) times higher than that in controls(Table III). Twenty percent of the cases

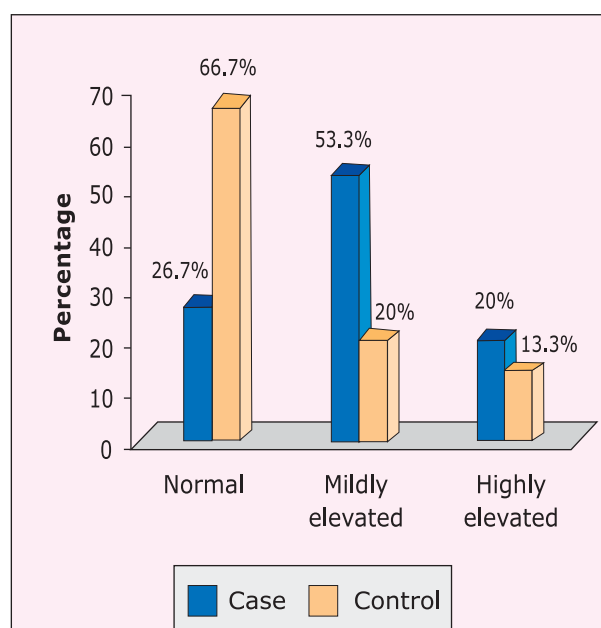
had highly elevated and 53.3% mildly elevated LDL as compared to 13.3% and 20% of controls respectively (Fig.1).

**TABLE III. Risk of developing elevated LDL in case group compared to control group**

Level of LDL (mg/dl)	Group		Odds Ratio (95% CI of OR)	p-value
	Case (n = 60)	Control (n = 60)		
>130 (Raised)	44(73.3)	20(33.3)	5.5(2.5-12.1)	<0.001
$\leq$ 130 (Normal)	16(26.7)	40(66.7)		

Figures in the parentheses indicate corresponding %;

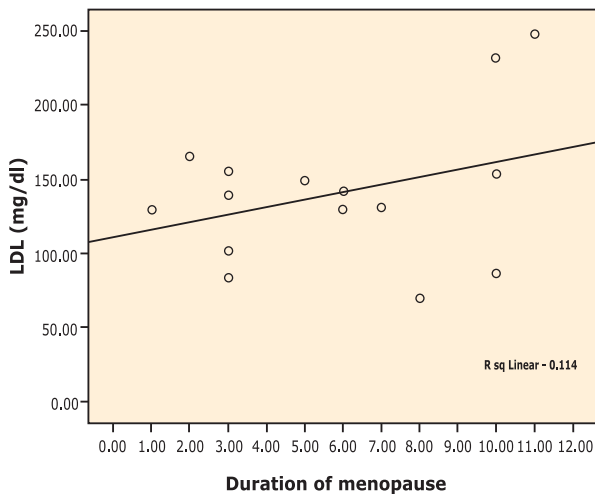
\*Chi-squared Test ( $\chi^2$ ) was done to analyse the data.



**FIGURE 1:** Distribution of LDL cholesterol among the study subjects (n=120)

#### Correlation between duration of menopause and LDL.

The correlation between duration of menopause and serum LDL level shows that the two variables bear linear relationship ( $r = +0.338$ ,  $p = 0.008$ ) (Fig. 2).



**FIGURE 2:** Relationship between duration of menopause and serum LDL level

## DISCUSSION

The present study demonstrated that 20% of the postmenopausal women had highly elevated level of LDL, 53.3% mildly elevated and the rest (26.7%) had normal level of LDL, where as 13.3% of premenopausal women had highly elevated, 20% mildly elevated and 66.7% normal level of LDL. The risk of having elevated level of LDL in postmenopausal women was estimated to be 5.5-fold (95% CI = 2.5 - 12.1) higher than that in premenopausal women. The serum total cholesterol was also much higher in postmenopausal women (212.3 mg/dl) than that in their premenopausal counterparts (186.3 mg/dl) ( $p = 0.002$ ) which supports the hypothesis that menopause reduces the level of oestrogens, which in turn, causes abnormal changes in serum lipid. The duration of menopause and LDL level showed a linear relationship ( $p = +0.338$ ,  $p = 0.008$ ) indicating that longer the duration of menopause the greater is the chance of having elevated LDL level. The later finding further fortifies the concept that menopause raises the level of LDL

including changes in other lipids as well. Varu et al.<sup>9</sup> showed that serum LDL level significantly increased with increase in the duration of menopause.

Consistent with the findings of our study, Chen & Huang<sup>10</sup> showed in their study that total cholesterol and LDL were higher in postmenopausal women than those in premenopausal women. Shende et al.<sup>11</sup> showed significant rise of serum total cholesterol, TG, LDL-C and VLDL-C in postmenopausal women compared to those in pre-menopausal women ( $p < 0.001$ ).

According to Arca et al.<sup>12</sup> decrease in estrogen secretion with the cessation of ovarian function probably contribute to higher LDL cholesterol level in postmenopausal women. Higher TC, TG and LDL levels were also found in post menopausal woman than in premenopausal.<sup>13</sup> The concentration of the various subclasses of cholesterol, LDL-C and TG were significantly higher and HDL-C lower in women greater than 45 years of age when compared to women below 45 years age.<sup>14</sup> Estrogen increases hepatic synthesis of LDL cholesterol receptor for Apo- $\beta$  100 resulting in increased LDL cholesterol uptake and thereby decreases circulating LDL levels. Thus its deficiency results in rise in LDL cholesterol in postmenopausal women.

## CONCLUSION

Summarizing the findings of the study, it appears that postmenopausal women are at increased risk of having higher LDL cholesterol than the premenopausal women and the level increases linearly with the corresponding duration of menopause. So screening the postmenopausal women for lipid profile will have utmost implication in preventing the diseases or consequences of altered lipid profile like coronary heart disease.

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