Correlation Between Serum Malondialdehyde (MDA) Levels and Lipid Profile in Menopausal Women in Dr. Pirngadi Hospital Medan

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ABSTRACT

Background: Menopause is a condition of permanent cessation of menstrual cycle due to loss of ovarian activity resulting in a decrease in estrogen, as a result, metabolic changes can occur such as dyslipidemia. In addition, decreased estrogen levels have been shown to increase oxidative stress in the body. Malondialdehyde is a marker of oxidative stress and can be monitored as a developmental predictor of atherosclerosis. It is also known that menopausal women are more prone to experiencing dyslipidemia which can trigger coronary heart disease**.**

Objective: Analyze the correlation between serum MDA levels with lipid profiles in menopausal women in
Methods: This research is an observational descriptive study with a case series design in which case are nurses and midwives who have menopause naturally in Dr. Pirngadi Hospital, North Sumatra, Indonesia. Data is collected from January 2020 until the sample is fulfilled. This study used a sample of 31 people by consecutive sampling. Subjects were performed anamnesis and body mass index (BMI) measurements. Serum MDA levels and lipid profiles were examined by laboratory tests of venous blood using the ELISA (Enzyme Linked Immunosorbent Assay) method. Then data is collected and analyzed using statistical analysis**.**

Results: In this study a positive correlation was obtained between serum MDA levels and total cholesterol levels ($p = 0.024$; $r = 0.403$), LDL ($p = 0.019$; $r = 0.418$), and triglycerides ($p = 0.040$; $r = 0.317$) in postmenopausal women. However, no significant correlation was found between serum MDA levels and HDL ($p = 0.393$; $r = -0.159$). There is a correlation between serum MDA levels with duration of menopause ($p = 0.004$; $r = 0.499$). There is a correlation between serum MDA levels with BMI ($p = 0.002$; $r = 0.532$).

Conclusion: The higher the serum MDA level, the higher the total cholesterol, LDL, and triglyceride levels. However, there is no correlation between serum MDA levels and HDL levels. There is a correlation between serum MDA levels with duration of menopause and BMI

Keywords : serum malondialdehyde, menopause, lipid profile , BMI.

Introduction

According to the World Health Organization (WHO), menopause is the cessation of menstruation permanently due to physiological changes due to loss of follicular ovarian activity. Menopause is defined as the absence of menstruation for 12 consecutive months without any physiological or pathological causes. This occurs when the ovaries stop releasing eggs or the ovaries have been removed and the amount of the hormone estrogen in the body decreases. Menopause can appear at various ages , starting from 40 years to over 50 years. In general, the average age of menopause is around 51 years[. 1 , 2,3,4]

Globally, the number of women over the age of 50 has increased due to an increase in life expectancy so there has also been an increase in the number of women of menopause. In Asia according to WHO, by 2025 the number of older women will increase from 107 million to 373 million. In 2016, in Indonesia reached 14 million menopausal women or 7 , 4 % of the total population. In Indonesia, by 2025 it is estimated that there will be 60 million menopausal women[. 5]

During the menopausal transition period women will experience a number of physiological changes. Based on several survey and research results in Indonesia, 70% of women aged 45 to 54 years tend to experience various symptoms such as hot flushes , sleep disorders, psychological disorders, sexual disorders, neurological disorders, bone and muscle pain, osteoporosis and cardiovascular disease. [2]

One of the highest morbidity and mortality rates due to menopause is cardiovascular disease. Facts according to the American Heart Association (AHA) say more than a third of adult women suffer from one form of cardiovascular disease, especially coronary heart

disease (CHD) and the number of deaths in women exceeds men. In 2012, around 56% of the causes of female deaths were cardiovascular disease and the most was CHD . It is said that before menopause women are less likely to develop CHD than men. But with increasing age and decreasing estrogen levels after menopause, the risk of heart disease increases . Therefore, screening of menopausal women at high risk for cardiovascular disease is important. [2 , 3,4]

Cardiovascular disease begins with the process of atherosclerotic plaque formation in blood vessels. At present, various studies form the hypothesis that malondialdehyde (MDA) has a relationship with the atherosclerotic process so that it is expected to help detect the risk of cardiovascular disease, such as CHD, stroke, type 2 diabetes mellitus, and metabolic syndrome. MDA itself is a product of lipid peroxidation that occurs due to increased oxidative stress. [6 , 7] Estrogen has a beneficial effect on endothelial dysfunction, modulates lipid profile and increases nitric oxide production. Decreased estrogen levels at menopause are manifested by several metabolic changes such as reduced glucose tolerance, dyslipidemia, oxidation-reduction status imbalance, changes in body fat distribution, hypertension, endothelial dysfunction, and inflammation of blood vessels. [6]

During menopause, changes in lipid levels and lipoprotein distribution cause an increase in CHD events. The main activity of lipids in tissues occurs both as free fatty acids released by adipose tissue and in the form of lipoprotein carriers , mainly formed by the liver and intestine (chylomicrons and very low density lipoprotein (VLDL) for triglycerides (TG), and low density lipoproteins (LDL)) and high-density lipoprotein (HDL) for cholesterol. [8]

Statisticall, menopausal women have a significant increase in total cholesterol and LDL levels and a significant decrease in HDL when compared to premenopausal women. Other studies showed that total cholesterol, LDL and MDA levels were significantly higher in the menopause group (2 , 61 ± 0.69 nmol / ml) than in the control group (1.66 ± 0.79 nmol / ml). MDA is positively correlated with total cholesterol (r = 0.572) and LDL in women (r = 0.690). Also found a significant correlation between the average age of women and the average value of MDA levels (r = 0.665). [30]

With research on one of the markers of oxidative stress in menopausal women, MDA can be monitored as a prognostic development of atherosclerosis. 13 In addition, it is also known that menopausal women are more prone to dyslipidemia also trigger CHD. As far as authors are concerned, to date there have been no studies that assess serum MDA levels in menopausal patients and their correlation with lipid profiles in North Sumatra. Therefore, researchers are interested in conducting this research.

Population and Sample

The population of this study was nurses or midwives who had menopause naturally at RSUD dr. Pirngadi Medan.The sample of the study was the majority of participants who were nurses or midwives at Medan Pirngadi Hospital who had gone through menopause who met the inclusion and exclusion criteria selected by consecutive sampling technique. There was 30 sample from this study.

Methods

This research is a descriptive study with a case series research design . This research was carried out at Dr. Pirngadi General Hospital Medan, for serum MDA examination carried out at the Integrated Laboratory of the Faculty of Medicine, University of North Sumatra and the Hospital Laboratory of the University of North Sumatra for the measurement of lipid profiles . This research was conducted in January 2020

Result

Table 1 Characteristics of the sample in the study

Characteristics	n	(%)	Mean ± SD
Age (years)			55 ± 2,5
45 – 50	2	6,5	
51 – 55	10	32,3	
56 – 60	19	61,3	
Age of menopause (years)			48,2 ± 2,5
Length of menopause (years)			7,2 ± 2,6
1 – 5	8	25,8	
6 – 10	21	67,7	
>10	2	6,5	
IMT			27,9 ± 3,2
BB <	0	0	
Normal	4	12,9	
BB >	21	67,7	
Obesciy	6	19,4	
Total	31	100,0	

Based on the table above, obtained characteristics of research subjects. Age of study subjects most often found in the age group 56-60 years (61 , 3 %) with mean age of study subjects was 55 ± 2.5 years. Based on the duration of menopause, the majority of research subjects had experienced menopause for 6-10 years, namely 21 people (67.7%) with a mean menopause duration of 7.2 ± 2.6 years and the average age at menopause was 48.2 ± 2, 5 Based on BMI the majority of subjects in this study were over 21 people (67 , 7 %) with an average BMI of 27.9 ± 3.2

Table 2. MDA Values and Lipid Profiles in Research

Variabel	Mean ± SD
Serum MDA levels (nmol/ml)	1,8 ± 0,8
Total cholesterol level (mg/dl)	207,5 ± 31,2
LDL level (mg/dl)	142,5 ± 30,3
HDL level(mg/dl)	54,8 ± 12,8
Trigliserida level (mg/dl)	106,9 ± 42,7

In this study, the mean serum MDA level in the study subjects was 1.8 ± 0.8 nmol / ml. And also obtained a mean lipid profile consisting of total cholesterol, LDL, HDL, and triglyceride levels, each of which is 207.5 ± 31.2 mg / dl, 142.5 ± 30.3 mg / dl, 54.8 ± 12 , 8 mg / dl, and 106.9 ± 42.7 mg / dl.

Table 3. Correlation between serum MDA levels with total cholesterol

Characteristics	r	*p*
MDA serum level Kolesterol level	0,403	0,024

[a] *Pearson*

Based on data analysis using Pearson correlation, the correlation coefficient (r) is 0.403 with a significance value (p) 0.024. From these results it can be concluded that there is a positive correlation between serum MDA levels with total cholesterol levels. The direction of the positive correlation shows that the higher the serum MDA level, the higher the total cholesterol level. Correlations obtained in this study indicate the strength of moderate correlation.

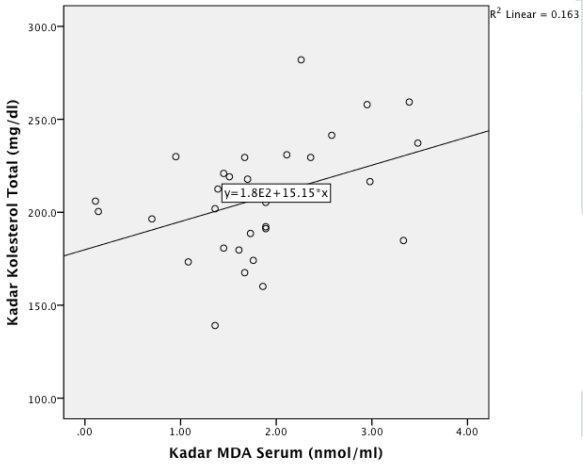

Figure 1. Correlation between serum MDA levels with total cholesterol

Table 4 Correlations between serum MDA levels with LDL

Characteristics	r	*p*
MDA serum level LDL	0,418	0,019

[a] *Pearson*

In the results of research with data analysis using Pearson correlation obtained r = 0.418 and p = 0.019. So it can be concluded that there is a correlation between serum MDA levels with LDL levels in the blood. The correlation strength is moderate and positive, which means that the higher the serum MDA level, the higher the LDL level

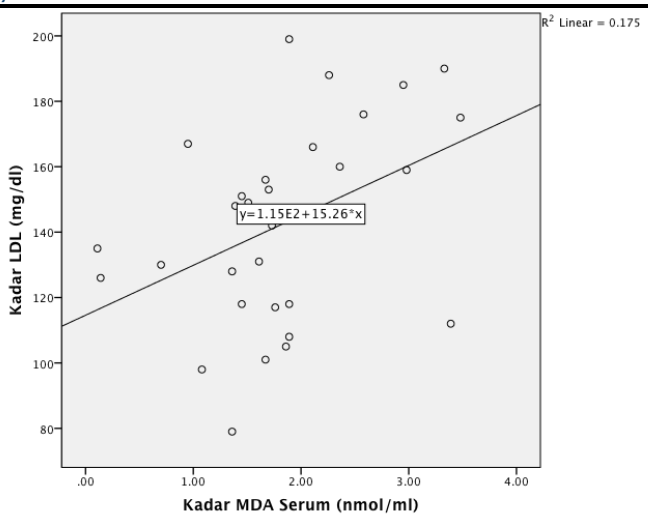

Figure 2. Correlation between serum MDA levels with LDL

Table 5. Correlation between serum MDA levels with HDL

Characteristics	R	*p*
MDA serum level HDL	-0,159	0,393

[a] *Spearman*

Based on statistical data analysis with Spearman's correlation on the relationship between serum MDA levels and HDL levels, p values = 0.393 and r = -0.159, which means there is no significant correlation between serum MDA levels and HDL levels.

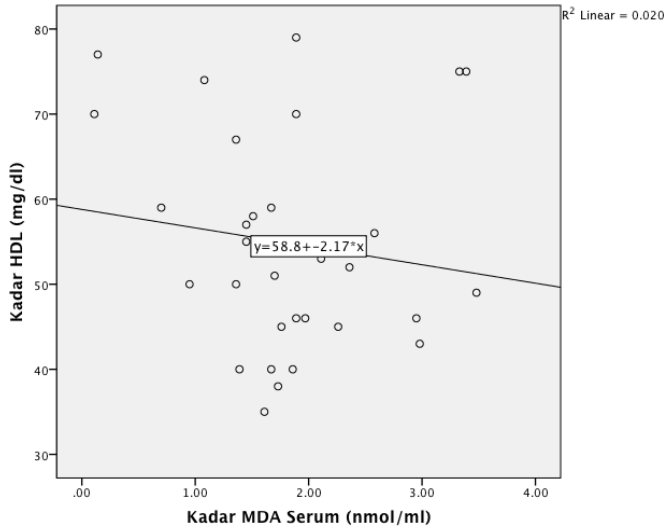

Figure 3. Correlation between serum MDA levels with HDL

Table 6. Correlation between serum MDA levels with triglycerides

Karakteristik	r	*p*
Kadar MDA serum Trigliserida	0,371	0,040

[a] *Pearson*

In table 6 based on data analysis with Pearson correlation, it can be concluded that there is a correlation between serum MDA levels with triglyceride levels, with weak correlations (r = 0.371) and positive patterns, which means the higher the serum MDA level, the higher the triglyceride levels. Results of statistical tests found a significant relationship between serum MDA levels with triglyceride levels (p = 0.040)

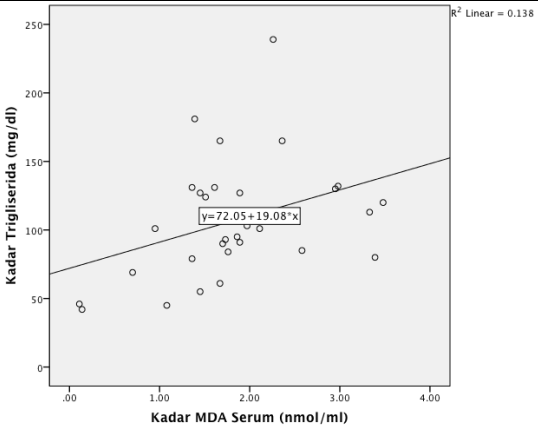

Figure 4. Correlation between serum MDA levels with triglyceride

Table 7 Correlations between menopause duration and serum MDA levels

Characteristics	r	*p*
MDA serum level Time of menopause	0,499	0,004

[a] *Pearson*

In the results of research with data analysis using Pearson correlation obtained r = 0.499 and p = 0.004. So it can be concluded that there is a correlation between serum MDA levels with menopause duration. The correlation strength is moderate and positive, which means the longer menopause, the higher the serum MDA level..

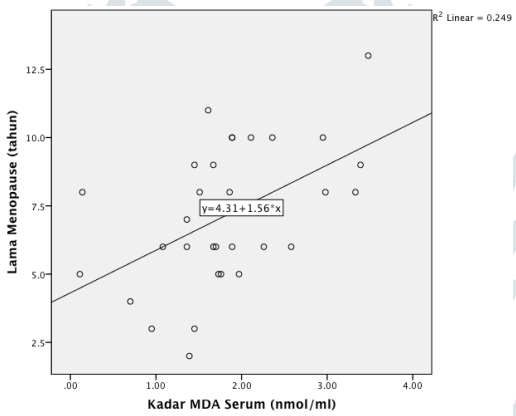

Figure 5. Correlation between menopause duration and serum MDA levels

Table 8. Correlation between BMI and serum MDA levels

Characteristics	r	*p*
MDA serum level IMT	0,532	0,002

[a] *Pearson*

In table 8 based on data analysis with Pearson correlation, it can be concluded that there is a correlation between serum MDA levels with BMI (p = 0 , 02) with moderate correlation strength (r = 0.532) and positive patterning which means the higher the serum BMI, the higher levels MDA serum.

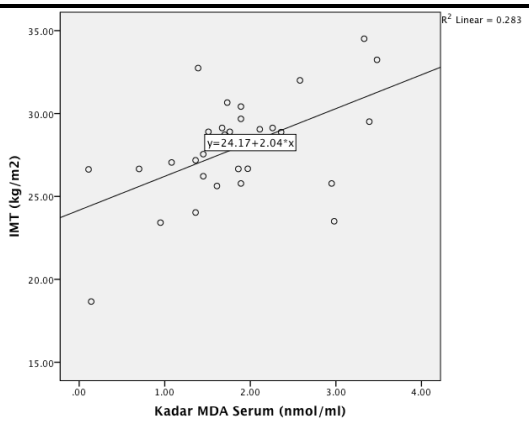

Figure 6. Correlation between BMI and serum MDA levels

Discussion

From the research the characteristics of the research subjects were obtained. Age of study subjects most often found in the age group 56-60 years (61 , 3 %) with mean age of study subjects was 55 ± 2.5 years. Based on the duration of menopause, the majority of research subjects have experienced menopause for 6-10 years, namely 21 people (67.7%) with a mean menopause duration of 7.2 ± 2.6 years, from this data we get the average age of menopause in the sample this study was 48.2 ± 2.5 years. Based on BMI the majority of subjects in this study were over 21 people (67 , 7 %) with an average BMI of 27.9 ± 3.2. In this study, the mean serum MDA level in the study subjects was 1.8 ± 0.8 nmol / ml. And also obtained a mean lipid profile consisting of total cholesterol levels 207.5 ± 31.2 mg / dl, LDL 142.5 ± 30.3 mg / dl, HDL 54.8 ± 12.8 mg / dl, and triglycerides 106 , 9 ± 42.7 mg / dl.

This is in accordance with the research of Onvural et al, in which in their study found the average age of menopause was 48.5 ± 5.7, the average total cholesterol level was 184.2 ± 36.7, LDL 110.1 ± 34, HDL 46.9 ± 9 , 0, triglycerides 140.2 ± 31.8 and MDA 1.35 ± 0.4. 30 In the Mallick et al study also found similar results where the mean age in their study sample was 46.91 ± 3.67, the average total cholesterol was 192.93 ± 32.97, Triglycerides 139.28 ± 51.08, HDL 41.40 ± 9.95, LDL 123.67 ± 32.02, MDA 5.99 ± 2.27. 17 Likewise in the study of S. Signorelli et al., Which obtained total cholesterol values in the study group of 223.59 ± 34.98, LDL-C 149.04 ± 31.70, Triglycerides 101.58 ± 3.65, MDA 0, 88 ± 0.004. [31]

From the results of this study based on data analysis using Pearson correlation, the correlation coefficient (r) is 0.403 with a significance value (p) 0.024) between serum MDA levels and total cholesterol levels. The direction of the positive correlation shows that the higher the serum MDA level, the higher the total cholesterol level. Correlations obtained in this study indicate the strength of moderate correlation.

These results are consistent with Onvural et al's study in which they found a correlation between MDA and total cholesterol levels (r = 0.572) 30 . This is consistent with the research of Nsonwu-Anyanwu et al, where they get a positive correlation between total cholesterol levels in the blood with MDA levels with a value of r = 0.336; p = 0.034. 36 This is also in line with the research of Asrullah et al, in which their study found an association between plasma MDA levels and total cholesterol levels in the blood (r = 0 , 87 , p = 0.05) 37 . However, research by Rao et al. Found no significant correlation between total cholesterol levels and MDA levels (r = 0.258, p = 0 , 09) 38 , this is likely due to differences in the research subjects, where in their study the research subjects were groups affected by infarction myocardial, regardless of sex. In the study of Atamer et al. also found no significant correlation between total cholesterol levels with MDA levels in the blood (r = 0.004; p = 0.98), this is likely due to differences in the research subjects, where their research subjects were a group of cases suffering from asymptomatic cholelithiasis. Research Manohar et al also found no correlation between total cholesterol levels and MDA levels in the blood (r = 0 , 22 ; p> 0.05) this is likely because their study subjects suffered from type 2 diabetes mellitus so it was not the same as the sample group in the study. [40]

In research with data analysis using Pearson correlation obtained the relationship of serum MDA levels with LDL levels in the blood. The correlation strength is moderate and positive, which means that the higher the level of serum MDA, the higher the LDL level (r = 0.418 and p = 0.019).

These results are in accordance with the research of Onvural et al. In which they found a correlation between serum MDA and LDL (r = 0.690) 30 . The Nsonwu-Anyanwu et al study, in their study found an association between LDL levels in the blood and MDA levels (r = 0.332; p = 0 , 0403) 36 . Signorelli et al also found a positive correlation between serum MDA levels and LDL (r = 0.30; p <0.03). 31 But the results of this study contradict the results of the study of Mnohar et al, where they found no correlation between LDL levels and MDA levels in the blood (r = 0.33; p = 0.28) 40 ; this also contradicts the results of the study of Rao et al. in which they found no correlation between LDL levels and MDA levels (r = 0.199; p = 0.20) 38 . Atamer et al in his study also did not find a significant relationship between LDL levels in the blood with MDA levels (r = 0.238; p = 0.139) 39 . Lipid peroxide comes from the oxidation of unsaturated double fatty acids and their esters which are capable of producing further lipid peroxide by free radical chain reactions. Among human plasma lipoproteins, LDL is most susceptible to peroxidation. Oxidative (modified) LDL has the effect of more easily penetrating plaque in blood vessel endothelium which causes an inflammatory response and plays a major role in atherosclerotic changes. [22 , 24]

Based on statistical data analysis with Spearman's correlation between serum MDA levels and HDL levels, p values = 0.393 and r = - 0.159, which means there is no significant correlation between serum MDA levels and HDL levels.

This is consistent with the research of Rao et al., Where they found that there was no relationship between HDL levels in the blood with MDA levels (r = 0.134; p = 0 , 04) 38 . Likewise in a study conducted by Manohar et al where they found no correlation between HDL levels in the blood with MDA levels in the blood (r = 0 , 21 ; p = 0.18) 40 . In the study of Atamer et al also found the same results where they did not find a significant correlation between HDL levels in the blood with MDA levels (r = 0.047; p = 0.773). 39 The results of this study are not in accordance with the results of the Nsonwu-Anyanwu et al study, where they found a significant correlation between HDL levels in the blood with MDA levels (r = 0.636; p <0.001) 36 , Nsonwu-Anyanwu et al reported a significant positive correlation strong levels of HDL with MDA, this is likely due to differences in age groups in this study, where their research was conducted on women of reproductive age while all samples in this study were menopausal women.

In this study, there was a correlation between serum MDA levels and triglyceride levels, with weak correlation (r = 0.371) and positive pattern, which means that the higher the serum MDA level, the higher the triglyceride levels. Results of statistical tests found a significant relationship between serum MDA levels with triglyceride levels (p = 0.040).

This is consistent with the research of Manohar et al. In which they found a significant relationship between triglyceride levels in the blood and MDA levels (r = 0 , 38 ; p <0.05), where in this study also found a weak relationship between triglyceride levels and MDA in the blood. 40 This study is also in line with the results of Rao et al's study, where they found a weak correlation between triglyceride levels and MDA levels (r = 0.365; p = 0.017). 36 These results contradict the results of the study by Atamer et al, in which in their study no correlation was found between triglyceride levels in the blood and MDA levels (r = 0.177; p = 0.276). [39]

In the results, it was found that there was a correlation between serum MDA levels and the length of menopause. The correlation strength is moderate and positive, which means that the longer the menopause, the higher the serum MDA level (r = 0.499 and p = 0.004).

These results are consistent with the research of Onvural et al. In which they found a correlation between MDA and age (r = 0.665) 30 . This is in accordance with the research of Bradley et al, where they found a significant relationship between plasma MDA levels and increased age (r = 0.6; p <0.05) 41 , this is also in accordance with Signorelli's study in which the age of menopause has a correlation positive with MDA levels (r = 0.34, p <0.05), 31 but in this study it was not explained regarding the sample criteria used. The results of this study are not in accordance with the results of the study of Massudi et al, where they did not find any correlation between MDA and menopause duration (r = 0.20; p = 0.37) while in men there was a positive correlation between MDA and age, where the higher age, the higher the MDA level (r = 0.62; p = 0.004). 42 Reduction of estrogen levels in menopausal women is believed to be a factor in the development of oxidative stress, and the release of free radicals or reactive oxygen species (ROS) which are the cause of various pathologies. Estrogen has been shown to have antioxidant properties so that estrogen deficiency causes susceptibility to oxidative damage. This might explain in part, the significantly higher serum MDA level in the menopause group. [43]

In this study found a correlation between serum MDA levels with BMI, with a moderate correlation (r = 0.532) and positive patterned which means that the higher the BMI, the higher the MDA level. Results of statistical tests found a significant relationship between serum MDA levels with triglyceride levels (p = 0 , 02).

These results are consistent with the research of Signorelli et al. In which they found a correlation of BMI with serum MDA levels (r = 0.34; p <0.05). 31 In line with the research of Altoum et al, where they found a significant relationship between BMI and serum MDA levels (r = 0.6; p <0.05) 44 , this is also consistent with An Huimei et al's study where BMI has a positive correlation with MDA levels (r = 0.33, p <0.05). 45 Obesity is substantially influenced by genetic, demographic, social and behavioral factors. Aging and menopause are associated with changes in adipose tissue metabolism that contribute to the accumulation of body fat after menopause.

Conclusion

The higher the serum MDA level, the higher the total cholesterol, LDL, and triglyceride levels. However, there is no correlation between serum MDA levels and HDL levels. There is a correlation between serum MDA levels with menopause duration and BMI.

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