

A Study of Myeloperoxidase and Lipid Profile in Obese Individuals

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ABSTRACT

Aim: To measure myeloperoxidase in obese subjects, who usually have deranged lipid profile, and to observe the association of myeloperoxidase with obesity as an early predictor of oxidative stress to prevent atherosclerotic cardiovascular diseases.

Methods: Twenty five obese subjects having a BMI $\geq 30 \text{ kg/m}^2$ and 25 controls with a BMI $\leq 24.9 \text{ kg/m}^2$, both males and females were taken.

Results: Obese group had a mean serum MPO level of $207.96 \pm 44.28 \text{ ng/ml}$ which was significantly ($P < 0.001$) higher than the controls who had mean serum MPO level of $80.04 \pm 24.8 \text{ ng/ml}$. Serum Cholesterol, Triglycerides and LDL of obese group was significantly higher than the control group. MPO showed significantly ($p < 0.05$) positive correlation ($r = 0.487$) with age in the control group. MPO showed a significant positive correlation with cholesterol, triglycerides and LDL in the obese group.

Conclusion: The study concludes that serum MPO levels are raised in obese individuals. This indicates that MPO is associated with increased oxidative stress as in obesity. MPO is also significantly correlated with cholesterol, triglycerides and LDL. All these factors therefore indicate that obesity may be associated with increased risk of atherosclerosis.

Key words: Myeloperoxidase, Lipid Profile, Obese Individuals

INTRODUCTION

Myeloperoxidase is a member of mammalian heme peroxidase super family and is stored within the azurophilic granules of leukocytes. MPO is found within circulating neutrophils, monocytes and some tissue macrophage population². This microbicidal enzyme is released when leukocyte activation and degranulation occurs³. The catalytic activity of MPO results in the generation of various reactive oxidants and diffusible radical species. These products play an important role in killing invading parasites and pathogens¹.

Myeloperoxidase has emerged as a potential participant in the promotion and propagation of atherosclerosis. It is linked to events that participate in the initiation and progression of plaque formation including lipid peroxidation, generation of atherogenic lipoproteins and dysfunctional HDL and catalytic consumption of nitric oxide. MPO may thus contribute to endothelial dysfunction, leukocyte transmigration and accumulation of foam cells⁴. Myeloperoxidase generates numerous reactive oxidants and diffusible radical species that are capable of initiating lipid peroxidation⁵ and promoting an array of post translational modifications to target proteins including halogenation, nitration and oxidative cross linking⁶.

Lipid peroxidation and protein nitration convert LDL into a high uptake form that is avidly taken up by the macrophage scavenger receptor CD 36⁷. Myeloperoxidase is also linked to catalyze the carbamylation of LDL by which it becomes a ligand for the scavenger receptor SRA-1⁸. Thus MPO generates multiple high uptake forms of LDL which are involved in atherosclerotic plaque formation. It has also been suggested that MPO modifies apolipoprotein A-1 thus generating dysfunctional high-density lipoprotein (HDL)⁹.

Obesity; especially abdominal obesity is related with atherogenic lipid profile i.e. high LDL cholesterol, VLDL and triglycerides with decreased HDL¹⁰. Oxidative stress is evident in obesity which plays central role in the development of atherosclerosis, Enzymatic sources of excess reactive oxygen species within vasculature include MPO which produces hypochlorous acid, Xanthine oxidase and NADP oxidase which produces super oxide ($\cdot\text{O}_2^-$) peroxy nitrite ($\cdot\text{ONOO}^-$) and nitryl chloride ($\text{NO}_2 \text{ Cl}$) which oxidatively modify lipids, proteins and DNA. At high levels these modifications may have damaging and pro-atherogenic effect¹¹.

MATERIAL AND METHODS

Twenty five (25) obese subjects having a BMI $\geq 30 \text{ kg/m}^2$ and 25 controls with a BMI $\leq 24.9 \text{ kg/m}^2$, both males and females, were taken. They were aged between 35-65 years. Exclusion criteria were

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hypertensives, smokers, diabetics, renal disease patients, people taking lipid lowering drugs and having any other systemic illness/malignancy.

BMI was calculated after measuring height in centimeters and weight in kilograms. A 6ml venous blood sample was drawn for biochemical analysis. The biochemical tests included lipid profile (serum total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol) and MPO enzyme immunoassay. Serum total cholesterol, HDL and Triglycerides were performed on fully automated chemistry autoanalyzer Dimension-RXL by Dade Behring while LDL was calculated applying Friedwald formula. Myeloperoxidase was assayed using Enzyme Immunoassay (EIA), a "sandwich" ELISA, using Oxford Biochemical research MPO-EIA kit.

RESULTS

There were 14 males and 11 females in the obese subjects group while the control group comprised of 12 males and 13 females. Comparison of age, height, weight and BMI revealed that mean weight and BMI of obese group was significantly higher than the control group. Serum cholesterol, triglyceride and LDL level in the obese group was significantly higher in the obese group. Obese group had a mean serum MPO level of 207.96±44.28ng/ml which was significantly (P<0.001) higher than the controls who had mean serum MPO level of 80.04±24.8ng/ml. Pearson coefficient of correlation was calculated for serum MPO level with age, height, weight, BMI. Serum cholesterol, triglycerides, HDL and LDL. MPO showed significantly (p<0.05) positive correlation (r=0.487) with age in the control group. Myeloperoxidase showed a significant positive correlation with cholesterol, triglycerides and LDL in the obese group while no significant correlation was seen between these parameters in the control group.

Table 1: Comparison of age, height, weight and BMI of obese group and non-obese controls

	Obese group (n=25)	Non-obese controls (n=25)	P value
Age (yrs)	51.60±7.74	48.64±10.4	0.260
Height (cm)	165.48±4.82	164.76±4.6	0.593
Weight (kg)	91.00±8.01	62.10±6.3	0.000**
BMI (kg/m ²)	33.24±2.40	22.84±10.6	0.000**

**p <0.001 significantly higher as compared to controls

Table 2: Comparison of lipid profile and MPO of obese group and non-obese controls.

	Obese group (n=25)	Non-obese controls (n=25)	P value
Cholesterol (mg/dl)	214.76±40.37	135.20±46.3	0.000***
Triglycerides (mg/dl)	233.16±79.82	149.48±86.	0.001**
HDL (mg/dl)	43.96±8.52	54.04±19.1	0.020*
LDL (mg/dl)	124.08±39.54	51.04±27.9	0.000**
MPO (ng/ml)	207.96±44.28	80.04±24.8	0.000**

*p <0.05 significantly lower as compared to controls

**p <0.01 significantly higher as compared to controls

***p <0.001 significantly higher as compared to controls

Table 3: Correlation of MPO with age, height, weight and BMI. Coefficient of correlation (r) is given. Figure in parentheses indicate number of cases in each group.

	Obese group (n=25)	Non-obese controls (n=25)
MPO with age (yrs)	0.160	0.487
MPO with height (cm)	0.082	-0.026
MPO with weight (kg)	0.252	-0.050
MPO with BMI (kg/m ²)	0.224	-0.055

*p <0.05 significantly lower as compared to controls

Table 4: Correlation of MPO lipid profile. Coefficient of correlation (r) is given. Figure in parentheses indicate number of subjects in each group.

	Obese group (n=25)	Non-obese controls (n=25)
MPO with cholesterol	0.565**	-0.343
MPO with triglycerides	0.421*	-0.146
MPO with HDL	-0.335	-0.242
MPO with LDL	0.480*	-0.323

*p <0.05 significantly lower as compared to controls

**p <0.01 significantly higher as compared to subjects

DISCUSSION

Myeloperoxidase is a leukocyte derived enzyme generating reactive oxidant species that may be atherogenic⁴. Potential mechanisms that relate to MPO promoting vascular disease include the following: stimulating conversion of LDL to an atherogenic form, selectively modifying apo-lipoprotein A-1 and generating dysfunctional HDL, promoting endothelial dysfunction, promoting vulnerable plaque, promoting myocardial dysfunction and abnormal ventricular remodeling after myocardial infarction.

The present study was conducted to compare MPO levels in obese and non obese individuals. Furthermore, to find whether MPO was related to

obesity as oxidative stress increases in obesity and is an independent risk factor for atherosclerotic cardiovascular disease. Association of MPO with BMI and lipid profile was also observed. There were 25 obese subjects and 25 non-obese controls. The mean weight and BMI of the two groups was significantly different. Serum cholesterol, triglyceride and LDL in the obese group were significantly higher in the obese group as compared to the control group. It has been reported by previous researchers that serum cholesterol level is associated with high BMI¹⁰⁻¹³. Carr has reported hypertriglyceridemia in abdominal obesity¹⁴. Nieves et al have suggested that obesity favors the expression of phenotypes namely hypertension and dyslipidemia characterized by elevation in triglycerides, production of small dense LDL particles and reduced HDL cholesterol.¹⁵ National Health and Nutrition Examination Survey (NHANES) data has demonstrated that LDL cholesterol levels were higher in obese than non-obese individuals¹⁶. Serum HDL level was significantly lower in the obese group than the control group. A previous study explained that intra abdominal visceral fat is a negative correlate of HDL cholesterol¹⁷. Regarding MPO, it was observed that an obese subject has significantly higher MPO level as compared to their control counterparts. Ghanbari et al in a study has shown MPO to be elevated in obese people (BMI >30) as compared to non-obese.¹⁸ Gandley et al reported that people with BMI > 30 had elevated MPO in circulation.¹⁹ Vander et al have reported that the relationship between MPO and blood pressure was strongest under conditions associated with stress like obesity, low HDL, metabolic syndrome and type 2 diabetes²⁰. When MPO was correlated with age, a significant positive correlation was seen in the control group. Similar results were obtained by El-Bejjani et al who reported positive correlation of MPO with age in general population²¹.

A highly significant positive correlation was observed between MPO and lipid profile except for HDL. Similar positive correlation of MPO with cholesterol, triglyceride and LDL has been reported^{22,23,24}. Myeloperoxidase exhibited a non-significant negative correlation with HDL in all groups. A significant but negative correlation of MPO with HDL was reported by Zhang et al and Exner et al^{25,26}.

CONCLUSION

The study concludes that serum MPO levels are raised in obese individuals (BMI>30kg/m²). This indicates that MPO is associated, increased oxidative stress as in obesity. MPO is also significantly correlated with cholesterol, Triglyceride and LDL. All

these factors therefore indicate that obesity may be associated with increased risk of atherosclerosis.

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