*Research Article*

# EFFECTS OF TWELVE WEEKS OF SWIMMING EXERCISE PROGRAM ON HEPATIC AND CARDIAC OXIDATIVE STATUS, LIVER FUNCTIONS AND SOME CARDIOVASCULAR RISK FACTORS IN A RAT MODEL OF HIGH FAT DIET-INDUCED OBESITY

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## Abstract
**Background:** The induction of obesity may be perfor-med in animals by neuroendocrine, dietary or genetic changes. This study was designed to investigate the effect of ١٢ weeks' exercise program on weight loss, liver functions and oxidative state of the liver and heart in both obese and non-obese rats. **Methods:** Obesity was induced by using high fat diet (HFD) and then rats were randomly divided into four equal groups (٦ rats each); normal, trained normal, obese and trained obese groups. Blood samples were taken for measurement of lipid profile and liver transaminases. Tissue samples from liver and heart were also taken for determination of malondialdehyde (MDA) content and total antioxidant capacity. **Results**: feeding the rats HFD diet significantly increased final body weight, liver transaminases and induced a state of dyslipideamia. Hepatic and cardiac tissues of obese rats also showed significantly higher MDA and lower total antioxidant capacity (TAC) levels than the normal non-obese group. On the other hand, exercise training successfully minimized the HFD-induced adverse effects on body weight, lipid profile and improved the antioxidant capacity in both hepatic and cardiac tissues. **Conclusion:** obesity could have deleterious effects on different body organs including heart and liver. In the present study, obese rats showed disturbed lipid profile, liver function and oxidant-antioxidant status in both the liver and the heart, which were all improved following chronic exercise training.
**Keywords:** Obesity, High fat diet, Liver, Heart, Malondialdehyde and Total antioxidant capacity

## Introduction
Obesity is a pathological condition in which excess body fat has accumulated to the extent that it may have an adverse effect on health, leading to reduced life expectancy and/or increased health problems(١). The induction of obesity may be perfor-med in animals by neuroendocrine, dietary or genetic changes. The great similarity and homology between the genomes of rodents and humans make these animal models a major tool to study obesity. Obesity affects many organs in the body such as liver, heart and kidney(٣).

Obesity is associated with the appearance of systemic metabolic disorders, such as glucose intolerance, increased triglyceridemia, high density lipoprotein (HDL)-cholesterol reduction and arterial hypertension. These disorders are highly associated with cardiovascular disease

This association is known as metabolic syndrome. Metabolic syndrome patients may also exhibit a state of chronic inflammation caused by an increased dependence on lipids as an energy source, which leads to the formation of oxygen reactive species and subsequent cell damage and protein structure disarray(٢).

The Liver is the largest and most complex internal organ in the body. The Liver is involved in several vital functions, such as metabolism, secretion and storage(٤). Consumption of a caloricrich diet results in lipid accumulation, excess production of inflamm-atory cytokines,

and macrophage infiltration that favors the progression of liver disease[٥].

It is apparent that a variety of adaptations and/or alterations in cardiac structure and function occur as excessive adipose tissue accumulates, even in the absence of systemic hypertension or underlying organic heart disease this increases the risk of sudden cardiac death with obesity[٦].

Regular exercise has been reported to reduce the risk of diabetes mellitus (DM), hypertension (HT), obesity, CVD, and metabolic syndome[٧]. On the other hand, evidence has emerged that exercise training has anti-inflammatory effects, with minimal side effects, which have been shown to occur in several tissues, including skeletal muscle, adipose tissue, and probably the liver. In rats, exercise training lowers adipose tissue inflammation, suggesting that exercise may be a useful therapy. Lifestyle interventions involving exercise clearly improve insulin sensitivity, and possibly inflammation, in obese individuals; yet the mechanisms for these effects are not well understood[٨].

Therefore, the present study was designed to investigate the effects of high fat diet-induced obesity on rat liver functions and oxidative status of the liver and heart by measuring liver transaminases, serum lipid profile and oxidant-antioxidant status in order to shed light on the possible adverse effects of obesity on these organs. Also, an important question to this discussion is: "Can long term swimming exercise alleviate high fat diet-induced hepatic and cardiac complications?"

## Subjects and Methods

***I. Animals:***

Adult male albino (Sprague dawley strain) rats, about ٤ months old were used throughout the present study. Rats were purchased from the National Research Center, Cairo, Egypt. All animals were housed in stainless steel cages offering individual housing. Each rat had a tag number. They were left freely wandering in their cages for two weeks with normal hour's dark: light cycle for acclimaization before starting the experiment. All the procedures followed with the rats were in accordance with our institutional guidelines. The ethics protocol was approved by The Laboratory Animals Maintenance and Usage Committee of Faculty of Medicine in Minia University.

The rats were randomly classified into the following two main categories (١٢ rats in each): normal non-obese rats and obese groups. The first received standard diet while, the other received HFD for ١٢ weeks. After the ١٢ weeks of diet regimens, Li index was calculated for each rat according to the following formula;

Cube root of body wt (g) X ١٠ / nasoanal length (mm)

All rats fed with HFD had a Lee index higher than ٣ and were considered obese[٩]. Finally, rats were further divided into the following groups (٦ rats each):

١. ***Non-trained normal group***: rats were fed a commercially available standard diet for further ١٢ weeks.
٢. ***Trained (Exercised) normal group***: rats were fed a standard diet with concurrent exercise training for further ١٢ weeks.
٣. ***Non-trained obese group***: rats were fed a HFD for further ١٢ weeks.
٤. ***Trained (Exercised) obese group***: obese rats were fed a HFD with concurrent exercise training for further ١٢ weeks.

***II. Diet protocol*:**

The composition of experimental diet (g/kg diet) was according to the formula of Noeman et al., (٢٠١١)[١٠]. It included the standard diet for control rats (Fat ٥٪ [corn oil ٥٪], carbohy-drates ٦٥٪ [corn starch ١٥٪ and sucrose ٥٠٪], proteins ٢٠.٣٪ [casein ٢٠٪ and DL-Methionine ٣٪], fiber ٥٪, salt mixture ٣.٧٪, and vitamin mixture ١٪). The HFD contained (fat ٤٦٪ [corn oil ٢٥.٥٪, and beef tallow ٢٠.٥٪], carbohydrates ٢٤٪ [corn starch ٦٪ and sucrose ١٨٪], proteins ٢٠.٣٪ [casein ٢٠٪ and DL-Methionine ٣٪], fiber ٥٪, salt mixture ٣.٧٪, and vitamin mixture ١٪). Normal and HFD constituents were purchased from El-Gomhoria Company, Cairo, Egypt. HFD was preserved at ٤°C until used. Obesity was induced in ١٢ weeks.

***III. Exercise protocol:***

At the beginning of the program, the rats were given the chance to stay in water bath for a short time in few numbers. After becoming familiar with water, rats were put in water bath in large numbers and were urged to swim actively all the time. We did not use any sinker to increase exercise intensity as we found in pilot experiments that animals swam continuously to stay on the water surface. Rats in trained groups were exercised by swimming ١h/day, ٤times/ week for ١٢ weeks. The swimming exercise was performed in plastic barrel (٥٠cm) diameter filled with water (٥٠ cm deep) maintained at ٣٢-٣٦°C[١٠].

***IV. Body mass index (BMI):***

Body length (nose-to-anus length) was determined in all rats. The measurements were done in anaesthetized rats with light ether. Using a ruler to measure body length, this is considered to be the distance between the bottoms of the lower incisors to the anus from ventral surface. Rats were weighed using electronic balance.

All rats were weighed and their nose to tail length was measured and BMI was calculated weekly.

The body weight and length were used to determine BMI according to the following formula:-

Body mass index (BMI) = body weight (g)/length$^{٢}$ (cm$^{٢}$).

As considered by Novelli et al., (٢٠٠٧)[١١], a significant increase in BMI in comparison to a control is a marker of obesity and also obesity is usually taken as any significant increase in body weight or energy content relative to control animals. This was also according to Li et al., (٢٠٠٨)[١٢].

***V. Sample collection:***

At the end of the experimental period, all rats were sacrificed and blood samples were collected. Sera were separated and stored in aliquots at -٨٠°C till used for estimation of lipid profile including; total cholesterol (TC), triglycerides (TGs), low density lipoprotein (LDL), and high density lipoprotein (HDL) and liver transaminases including; Alanine transa-minase (ALT) and Aspartate transaminase (AST), by enzymatic colorimetric methods using commercial kits (Biodiagnostic, Egypt). Then the abdomen and the thorax were opened and both liver and heart were removed, washed three times in ice cold saline and blotted individually on ash-free filter paper, used for preparation of tissue homogenates for estimation of tissue MDA and TAC.

***VI. Preparation of tissue homogenates***

Specimens from each organ were weighed and homogenized separately in potassium phosphate buffer ١٠ mM pH (٧.٤). The ratio of tissue weight to homogenization buffer was ١:١٠. The homogenates were centrifuged at ٥٠٠٠ rpm for ١٠ min at ٤°C. The resulting supernatant was used for determination of MDA according to the method of Ohkawa et al., (١٩٧٩)[١٣] and TAC using colorimetric assay kit according to the manu-facturer's instructions (Biodiagnostic, Egypt).

**Statistical analysis**

Data were represented as means ± standard errors of the mean (SEM). Statistical analysis was performed using Graph pad Prism ٥ software and significant difference between groups was done by one-way ANOVA followed by Tukey-Kramar post hoc test for multiple comparisons with a value of $P \leq ٠.٠٥$ considered statistically significant.

## Results

*١. Changes in Body Mass Index (BMI) in different studied groups.*

The pre-exercise body mass index (BMI) was significantly higher in obese than non-obese rats. After termi-nation of the ١٢-week training program, the post exercise BMI was significantly different among all the experimental groups, recording the highest mean value (٠.٨٨±٠.٠٢ g/cm$^{٢}$, $P \leq ٠.٠٥$) in the obese non-trained rats, while the lowest mean value was recoded in the trained normal rats (٠.٥١±٠.٠١ g/cm$^{٢}$, $P \leq ٠.٠٥$). also, the post exercise BMI of the obese trained group was signicantly lower (٠.٧٥±٠.٠٢ g/cm$^{٢}$, $P \leq ٠.٠٥$) than that of the corresponding obese non-trained group reaching nearly the value of the normal non-obese group (٠.٧٠± ٠.٠٣g/cm$^{٢}$, $P \leq ٠.٠٥$), (Table ١).

**Table ١: Changes in body mass index (BMI) (g\cm$^{٢}$) in different studied groups.**

| Groups | Normal body weight group | | Obese group | |
|---|---|---|---|---|
| BMI (g\cm$^{٢}$) | Non-trained | Trained | Non-trained | Trained |
| BMI (pre-exercise) | ٠.٥٢ ± ٠.٠١ | ٠.٥٣ ± ٠.٠١ | ٠.٦٩ ± ٠.٠٢●* | ٠.٦٨ ± ٠.٠٢●* |
| BMI (post exercise) | ٠.٧٥ ± ٠.٠٢ | ٠.٥١ ± ٠.٠١● | ٠.٨٨ ± ٠.٠٢●* | ٠.٧٠ ± ٠.٠٣○* |

Data are expressed as mean ± S.E.M. of ٦ rats in each group.
●: Significant from normal body weight group.
○: Significant from obese group.
*: Significant from trained normal group.

*٢. Changes in serum levels of lipid profile in different experimental groups.*

The TC level was highest in obese non-trained rats among all experimental groups reaching a mean value of (١٨٩.٥ ± ٨.٧٢ mg/dl, P ≤ ٠.٠٥) and was lowest in the normal trained group (٦٤.٥٣ ± ٣.١٨ mg/dl, P ≤ ٠.٠٥). In obese trained rats, TC level was significantly lowered (٨٨.٨ ± ٣.٣٩ mg/dl, P ≤ ٠.٠٥) as compared to the corresponding obese non-trained group and almost reaching the normal level. But, it remained significantly higher than that of the normal trained rats (Table ٢).

The same as TC, TGs level was highest in obese non-trained group (٤٢٥.٦ ± ١٢.٩٦ mg/dl, P ≤ ٠.٠٥) and lowest in the normal trained group (١٢١.٠ ± ٦.٨٢ mg/dl, P ≤ ٠.٠٥) among all experimental groups. In obese trained rats, TGs level was significantly lower (٢١٦.٣ ± ٧.٧٩ mg/dl, P ≤ ٠.٠٥) than the corresponding obese non-trained group and almost reaching the normal level. But, it was still significantly higher than that of the normal trained group (Table ٢).

As regards HDL, the lowest mean value (٢٣.١٣±١.٦١ mg/dl, P ≤ ٠.٠٥) was recorded in the obese non trained rats among all the experimental groups. In addition, serum HDL level was significantly higher (٣٣.٦٦ ±١.٥٧ mg/dl, P ≤ ٠.٠٥) in obese trained rats than the corresponding obese non-trained rats but, insignificantly different from that of normal non-trained group (Table ٢).

On the contrary, LDL serum mean level was highest (١١٢.٢ ± ٦.٣٩ mg/dl, P ≤ ٠.٠٥) in obese non-trained group among all experimental groups and lowest (٢٨.٤١± ٢.٥٧ mg/dl, P ≤ ٠.٠٥) in normal trained group. Training program to the obese rats significantly lowered the serum LDL level (٥٦.٦٩±٢.٨٨ mg/dl, P ≤ ٠.٠٥) as compared to the corresponding obese non-trained group, but not to the normal level (Table ٢).

**Table ٢: Serum levels of lipid profile in different studied groups (mg/dl)**

| Groups / Parameters | Normal body weight group | | Obese group | |
|---|---|---|---|---|
| | Non-trained | Trained | Non-trained | Trained |
| TC (mg/dl) | ٩٣.١٦ ± ٤.٦١ | ٦٤.٥٣ ± ٣.١٨● | ١٨٩.٥ ± ٨.٧٢●* | ٨٨.٨ ± ٣.٣٩○* |
| TGs (mg/dl) | ١٩٨.٢ ± ٨.٧٥ | ١٢١.٠ ± ٦.٨٢● | ٤٢٥.٦ ± ١٢.٩٦●* | ٢١٦.٣ ± ٧.٧٩○* |
| HDL (mg/dl) | ٣٣.٩٢ ± ١.٤٢ | ٣٦.٣٥ ± ١.٥١ | ٢٣.١٣ ± ١.٦١●* | ٣٣.٦٦ ± ١.٥٧○ |
| LDL (mg/dl) | ٣٦.٧٥ ± ١.٥٨ | ٢٨.٤١ ± ٢.٥٧ | ١١٢.٢ ± ٦.٣٩●* | ٥٦.٦٩ ± ٢.٨٨●○* |

Data are expressed as mean ± S.E.M. of ٦ rats in each group.
●: Significant from normal body weight group.
○: Significant from obese group.
*: Significant from trained normal group.
TC: Total choloetrol; TGs: Triglycerides; HDL: High density lipoprotein;
LDL: Low density lipoprotein.

*٣. Changes in serum transaminases levels in different experimental groups.* As regards liver transaminases (ALT and AST), serum levels of both enzymes were highest (٣٥.٣٣ ± ٢.٧١ U/ml and ٤٦.٣٣ ± ٤.٢٦ U/ml, P ≤ ٠.٠٥, respectively) in obese non-trained rats among all the experimental groups.

Although training program to the normal non-obese rats did not alter significantly the serum levels of both ALT and AST, it significantly lowered their levels (١٤.٦٣±١.٢٩ U/ml and ٢٦.٦٣±٣.٢٥ U/ml, P≤٠.٠٥, respectively) in obese trained rats when compared to the corresponding obese non-trained group (Table ٣).

**Table ٣: Serum levels of liver transaminases in different studied groups.**

| Groups / Parameters | Normal body weight group | | Obese group | |
|---|---|---|---|---|
| | Non-trained | Trained | Non-trained | Trained |
| ALT (U/ml) | ١٦.٢٨ ± ١.٦٦ | ١٥.٤٦ ± ١.٧٦ | ٣٥.٣٣ ± ٢.٧١●* | ١٤.٦٣ ± ١.٢٩○ |
| AST (U/ml) | ٢٣.٧١ ± ٣.٣٨ | ٢٤.٨٣ ± ٢.١٥● | ٤٦.٣٣ ± ٤.٢٦●* | ٢٦.٦٣ ± ٣.٢٥○ |

Data are expressed as mean ± S.E.M. of ٦ rats in each group.
●: Significant from normal body weight group.
○: Significant from obese group.
*: Significant from trained normal group.
ALT: Alanin transaminase; AST: Aspartate transaminase.

*٤. Changes in hepatic oxidative status in different experimental groups.*
Figure ١, ٢ show the changes in hepatic MDA and TAC levels in different experimental groups. In obese non-trained group, hepatic MDA mean level was highest (٥٢.٤٩ ±٤.٩٤ pg/mg tissue, P ≤ ٠.٠٥) while, hepatic TAC was lowest (٦.٣٣ ± ٠.٨٩ µM/mg tissue, P ≤ ٠.٠٥) among all studied groups. Although training of normal rats failed to produce any significant change in hepatic MDA or TAC levels as compared to the corresponding normal non-trained rats, it produced a significantly lower MDA (١٨.٨٠ ±١.٣١ pg/mg tissue, P ≤ ٠.٠٥) and a significantly higher TAC levels (١٩.٩٩±٢.٢٨ µM/mg tissue, P ≤ ٠.٠٥) in hepatic tissue of obese trained rats as compared to the corresponding obese non-trained group, reaching nearly the same levels as the normal group (Figure ١, ٢).

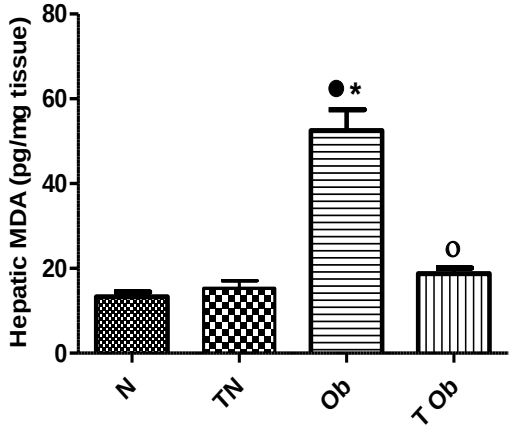


**Figure ١: hepatic MDA level in different experiment groups**. ●: Significant from normal body weight group; ○: Significant from obese group; *: Significant from trained normal group, P ≤ ٠.٠٥. N: Normal body weight; TN: Trained Normal; Ob: Obese; T Ob: Trained Obese.

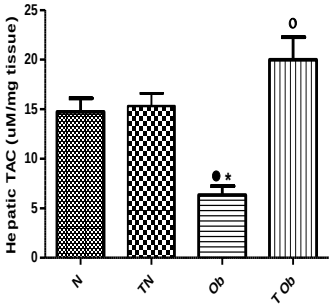


**Figure ٢: Hepatic TAC level in different experiment groups**. ●: Significant from normal body weight group; ○: Significant from obese group; *: Significant from trained normal group, P ≤ ٠.٠٥. N: Normal body weight; TN: Trained Normal; Ob: Obese; T Ob: Trained Obese.

*٣. Changes in cardiac oxidative status in different experimental groups.*

Figure (٣) shows the changes in cardiac MDA content in different experimental groups. The obese non-trained group recorded the highest MDA mean level (٢٧٧.٨ ± ٦.٦٢ pg/mg tissue, P ≤ ٠.٠٥) in the heart among all studied groups. Only, training of the obese but not the normal non-obese rats significantly lowered the cardiac MDA level (١٢٧.٣ ± ٨.٦٥ pg/mg tissue, P ≤ ٠.٠٥) as compared to the corres-ponding obese non-trained group but, it was still significantly higher than that of the non-trained normal group (٩٧.٢٨ ± ٥.٣٤ pg/mg tissue, P ≤ ٠.٠٥).

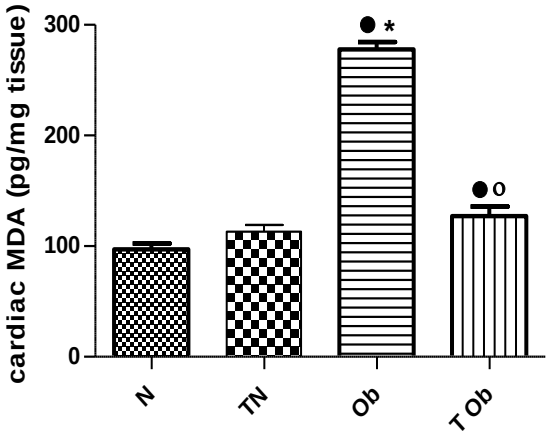


**Figure ٣: Cardiac MDA level in different experiment groups.** ●: Significant from normal body weight group; ○: Significant from obese group; *: Significant from trained normal group, P ≤ ٠.٠٥. N: Normal body weight; TN: Trained Normal; Ob: Obese; T Ob: Trained Obese.

On the contrary, the cardiac TAC mean level was lowest (٢٨.٦ ± ١.٧٦ µM/mg tissue, P ≤ ٠.٠٥) in obese non-trained group among all studied groups. Both trained obese and trained normal groups showed significantly higher levels of cardiac TAC (٤٤.٩٥ ± ٣.١٥ and ٦٨.٣٦ ± ٤.١١ µM/mg tissue, P ≤ ٠.٠٥) than the corresponding non-trained groups respectively, and reaching nearly the normal level (٥٣.١٣ ± ٣.١٨ µM/mg tissue, P ≤ ٠.٠٥) in case of trained obese rats (Figure ٤).

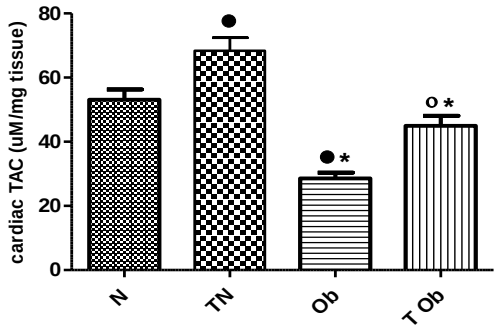


**Figure ٤: Cardiac TAC level in different experiment groups.** ●: Significant from normal body weight group; ○: Significant from obese group; *: Significant from trained normal group, P ≤ ٠.٠٥. N: Normal body weight; TN: Trained Normal; Ob: Obese; T Ob: Trained Obese.

## Discussion

Obesity has become an important worldwide health problem, with a rapidly increasing prevalence. Approximately ٧٪ of the estimated current world population is obese and two- to three-times more people than this are probably overweight.

The adverse clinical consequences of obesity are so harmful that a ٢٠٪ increase above the ideal weight is associated with a ٢٠٪ increase in the mortality rate[٣].

Feeding of HFD to rats was proved to be a useful model of putative effects of dietary fat in humans[١٤]. Rat models are therefore useful tools for inducing obesity as they will readily gain weight when fed HFD[٣]. In the present study, obesity was induced in male albino rats by using a HFD formula. Obesity was induced in ١٢ weeks. The weight gained by rats fed

HFD formula was significantly more than that gained by those fed the normal diet. Many workers were able to induce obesity in rats using different formulas of high fat diets[١٥]. It has been reported that rats fed with diet induced obesity gained ١٩٪ more weight because fat provides the substrates for trigylcerides accumulation and increase food intake[١٦].

In the present work, we found that administration of HFD is also associated with impairment in lipid profile in the form of significant increase in serum TC, TGs and LDL, and significant decrease in serum HDL levels as compared with normal group. These results agree with other previous studies[١٧,١٨]. The practice of regular physical exercise (swimming) in these animals could minimize the adverse effects caused by the chronic administration of HFD. Fatty acids and triglycerides in the fat and skeletal muscle are an important fuel during exercise of mild to moderate intensity, duration and prolonged fasting state[١٩]. Present data indicated that exercised rats receiving HFD significantly reduced serum TC and TGs, close to rats fed standard chow. An increase in energy expenditure during excerise might explain the reductions in the concentrations of these lipids[٢٠].

The highlight of the results observed in this study is that swimming exercise in rats fed with standard and high-fat diets led to reduction in body weight gain when compared with the sedentary groups. This fact may partially be due to the fact that during physical exercise; the skeletal muscle might increase its energy expenditure up to ١٠٠ times during physical exercise. The energy expenditure during long duration exercise performed at moderate intensity is obtained mostly by lipid mobilization, followed by carbohydrates and finally by proteins[٢٠]. So, triglyceride mobilization might explain the exercise-induced weight loss observed in trained animals at the end of the study which was confirmed by the

significantly decreased TGs level in both trained normal and obese groups.

Among other benefits, exercise stimulates lipolytic activity (with decreased plasma TG), promotes the use of free fatty acids (FFA) as an energy source and increases HDL concentration. Furthermore, favorable changes in the quantity and composition of LDL particles were also shown, as well as on the quality of HDL. The primary mediator mechanism of these changes seems to be the beneficial influence of regular exercise on the activity of peripheral enzymes, such as lipoprotein lipase (LPL), lecithin-cholesterol acyltransferase (LCAT) and hepatic lipase (HL). Physical exercise increases the number of capillaries and oxidative fibers in muscle, increasing lipolysis, which allows free flow of fatty acid to the tissue, reducing its concentration in plasma, which is an indicator of its uptake and oxidation by tissues[٢١] (Teixeira-Lemos et al., ٢٠١١).

Regular exercise is also able to activate an alternative pathway: the ٥' adenosine monophosphate-activated protein kinase (AMPK). This enzyme acts on the liver, muscle and adipocytes by increasing fatty acid oxidation, decreasing cholesterol synthesis, lipogenesis and lipolysis, and even modulating insulin secretion of pancreatic islets[٢٢] (Pold et al., ٢٠٠٥).

The liver functions as a buffer of lipids in the initial phase of a diet rich in animal fat and gradually releases them in circulation with the adaptation of this diet. The mechanisms for the development of non alcoholic fatty liver disease (NAFLD) are multiple and are associated with the unbalance of several cellular processes related to the signaling pathways of insulin, including the increased flow of FFA to the liver (lipolysis), de novo lipogenesis of free fatty acids, reduction of betaoxidation, mitochondrial dysfunction, oxidative stress, and endoplasmic reticulum[٢٣] (Postic and Girard, ٢٠٠٨). These alterations are related to the elevation of plasma liver enzymes, ALT, AST and Alkaline phosphatase (ALP)[٢٤] (Younossi, ٢٠٠٨). Exercise has a positive impact on body mass loss and has the potential to prevent the development of NAFLD independent of weight loss because it enhances the utilization of fat for energy production. Moreover, exercise has been used to promote oxidation of fats which is responsible for most of energy demand[١٩] (Marques et al., ٢٠١٠).

In the present investigation, the increased levels of AST and ALT have been observed in serum of high-fat fed rats compared to normal rats indicating the hepatotoxic effect of HFD. An elevation in the levels of serum marker enzymes is generally regarded as one of the most sensitive index of the hepatic damage. Observed elevated level of these enzymes in serum of HFD fed rats indicates that these elevations might be due to hepatocellular damage caused by HFD toxicity. These elevated enzymes in hepatocytes are usually released into the circulation causing an increase in their serum levels under hepatocellular injury or inflammation of the biliary tract cells[٢٥] (Uthandi and Ramasamy, ٢٠١١).

Another beneficial effect of physical training that was observed in the present study is related to the significant reductions in serum levels of AST and ALT as compared to the obese non trained group suggesting a hepatoprotective effect of exercise training in conditions such as obesity, as reported previously[٢٦] by Schultz et al. (٢٠١٢).

Lipid peroxidation is thought to be a component of obesity-induced pathology[٢٧] (Amirkhizi et al., ٢٠٠٧). The data presented in this study showed that obesity increased lipid peroxidation in hepatic and cardiac tissues as expressed by increased tissue levels of MDA. Our results are in basic agreement with the results of Olusi et al. (٢٠٠٢)[٢٨] and Amirkhizi et al. (٢٠٠٧)[٢٧] who showed that, obesity is an independent risk factor for increasing lipid peroxidation and decreased activity of cytoprotective enzymes.

Obesity can cause increased lipid peroxidation by progressive and cumulative cell injury resulting from pressure of the large body mass. Cell injury causes the release of cytokines, especially tumor necrosis factor alpha (TNF-a) which generates ROS from the tissues which in turn cause lipid peroxidation. Furthermore, the hypertriglyceridemia seen in obese rats may contribute to the alteration in the oxidant-antioxidant balance, suggesting that an increase in the bio-availability of free fatty acids could

eventually increase lipid peroxidation[١٠] (Noeman et al., ٢٠١١).

Lipid peroxidation in the heart leads to loss of the cellular membrane integrity due to oxidative modification of lipids and proteins that can ultimately lead to cardiac arrhythmias, poor contractility, infarction, cardiac failure or sudden death. The potential mechanism for increased lipid peroxidation in cardiac tissue may be due increased lipid substrate within the myocardium in which can serve as a larger target for oxidation by free radicals[٢٩] (Vincent et al., ٢٠٠١). It is well established that elevated myocardial work and mechanical overload is associated with increased free radical production consequently lipid peroxidation. Mechanical overload-induced increases in muscle oxygen consumption accelerate electron flux through the mitochondria in proportion to the need for ATP. This results in increased electron leakage from the electron transport chain and increased production of superoxide anions[١٠] (Noeman et al., ٢٠١١).

In the present study, exercise training alleviated the HFD-induced oxidative tissue injury in obese trained rats as evidenced by the significant reductions in hepatic and cardiac MDA levels and augmented both hepatic and cardiac TAC as compared to the obese non trained group. As regards the normal trained rats, cardiac but not hepatic TAC was higher than non trained rats suggesting a powerful antioxidant action of training on these organs.

Physical exercise might have improved the efficiency of lipid oxidation and the antioxidant status, which was diagnosed by means of total antioxidant activity in animal livers and hearts in trained groups. Maintenance of the antioxidant mechanism and a decrease in the structural damage caused by reactive oxygen species are very important for obese individuals. A steady high-level reactive oxygen species state could lead to cell structural damage, which, in turn, increases the concentrations of inflammatory markers such as TNF-a, inter-leukin ٦ and interferon-g and decreases the concentrations of adiponectin and anti-inflammatory interleukins[٣٠] (Franks, ٢٠٠٦). Maintenance of inflammation leads to the damaging effects present in metabolic syndrome, such as endothelial dysfunction and insulin resistance. Peroxidation of blood LDL cholesterol allows atheromatous plaques to accumulate on the endothelial walls, which might eventually detach and block blood flow in important small-caliber blood vessels, causing cerebrovascular accidents, myocardial ischemia and infarction[٣٠] (Botezelli et al., ٢٠١١).

Chronic exercise of moderate intensity (training) positively alters the oxidative homeostasis of cells and tissues, by decreasing the basal levels of oxidative damage and increasing resistance to oxidative stress. In fact, regular exercise causes adaptations in the antioxidant capacity, protecting cells against the harmful effects of oxidative stress, thus preventing cellular damage[٣١] (Urso and Clarkson, ٢٠٠٣). Adaptation to oxidative stress in trained individuals is clearly evidenced by a decrease in DNA damage, by sustained levels of protein oxidation and by an increment of resistance against chronic administration of hydrogen peroxide. Training is also able to alter the metabolism of purines, reducing the availability of substrate for xanthine oxidase (XO) in the trained muscle and plasma content of hypoxanthine and uric acid[٣١] **(**Teixeira-Lemos et al., ٢٠١١**).**

## Conclusion

The present work emphasizes the importance of the multifactorial nature of lifestyle changes, which influence lipid profile, liver functions and oxidative status of the liver and the heart. Since obesity is associated with dyslipidaemia, liver and heart impairments which may have a major contribution to morbidity and mortality. Weight intervention programs focused on physical exercise are of great importance in reducing the incidence of obesity-related risk factors such as atheroscterosis, coronary heart disease, and diabetes in addition to fatty liver. Further studies may be needed to identify other physical activity that can achieve improvement in these markers.

**Acknowledgement:**

It is difficult to translate our gratitude toward *Prof. Dr. Ibrahim Yahia Ibrahim*, head of Physiology Department, Faculty of Medicine, Minia University for his support and encouragement throughout this work. We would also like to express our deep appreciation and great thanks to *Prof. Dr. Saad Kamal Taha*,

Professor of Physiology, Faculty of Medicine, Al-Azhar University for his sincere help and encouragement throughout the study.

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