

Immune System Response to Aerobic Exercise Training in Obese Females

Azza Fekri Ismail*, Shehab M A. Kader*, Soheir Abo EL Fadel**,
Nashwa El Tablawy***

* Department of Physical Therapy for Cardiopulmonary Disorders and Geriatrics, Faculty of Physical Therapy, Cairo University

** Internal Medicine and *** Physiology Departments
Faculty of Medicine, Cairo University

ABSTRACT

Background: Obesity has a bad impact on immune system; on the other hand moderate exercise increases the resistance to infection. The aim of this study was to determine the response of complement system to aerobic exercise training in obese females. **Subjects and methods:** Thirty obese females participated in this study and they were divided randomly into two equal groups; the exercise group (group-1) which received aerobic exercise training for 4 months and the non-exercised group (group-2) which maintained their ordinary life style. Thirty age-matched non-obese females were the control group. Measurements of serum complement proteins (C3 and C4) were done at the start and at the end of the study, also the body mass index (BMI) was calculated at the start and at the end of the study. **Results:** at the start of the study; there was a significantly high levels of C3 & C4 in obese compared to the control (non-obese) females ($P=0.000$). At the end of the study; there was a significant decrease in BMI, C3 & C4 in the exercise group compared to the non-exercised group, also there was a significant differences between the measures at the start and at the end of the study in the exercise group as regards BMI, C3 & C4. **Conclusion:** obesity causes changes in the immune system as documented by increase in C3 & C4 levels. Moderate aerobic exercise produced weight reduction and decreased the abnormally elevated complement components (C3 & C4) in obese females; so improving the immune system.

Key words: complement system, aerobic exercise, immunity and obesity.

INTRODUCTION

Obesity has a serious effect on the immune system; fat tissue attracts immune system cells called macrophages that promote inflammation in the body. So if there is any extra fat, the body begins to produce an immune response similar

to the reaction against infection or injury¹. Recent study demonstrates that excessive activation of the classic pathway of complement commonly occurs in obesity, suggesting its possible role in adipose tissue inflammation and insulin resistance².

Complement was discovered many years ago as a heat-labile

component of normal plasma that augments the opsonization of bacteria by antibodies and allows antibodies to kill some bacteria. Complement proteins are produced constitutively by macrophages and hepatocytes, and are present in the circulation as inactive molecules. Several complement proteins are pro-enzymes. When activated, they become proteases that cut peptide bonds in other complement proteins to activate them in turn. Since each activated protease can activate many substrate molecules, the initial activation is rapidly amplified to produce millions of effectors molecules (a cascade) to opsonize pathogens and induce a series of inflammatory responses that help to fight infection. Complement C3 and C4 are the major plasma proteins of the immune system complement pathways. The synthesis of these proteins is increased in response to inflammation and infection³.

Previous studies have shown that several aspects of the metabolic syndrome, which in itself is tightly linked to visceral obesity, are associated with chronically elevated serum levels of acute-phase markers⁴. In particular, increased levels of C-reactive protein (CRP) and complement C3 can predict risk for future cardiovascular events, and both are negatively correlated with insulin sensitivity in obese subjects⁵⁻⁸. High C3 levels have been reported in subjects with diabetes and insulin resistance. The metabolic syndrome is associated with chronically elevated levels of several immune markers, some of which may have metabolic effects. The high expression of

complement genes in intra-abdominal adipose tissue might suggest that the complement system is involved in the development of visceral adiposity and/or contributes to the metabolic complications associated with increased visceral fat mass⁹.

Regular exercise has a favorable influence over many systems throughout the body and improves one's sense of well-being and general fitness. Much research has been carried out on the effects of exercise on immune and hormonal parameters in healthy individuals¹⁰. Several studies provide epidemiological evidence that regular exercise increases resistance to infections such as common cold whereas intense training is associated with increased upper respiratory tract infections¹¹. The aim of this study was to determine the response of complement system to aerobic exercise training in obese females.

SUBJECT & METHODS

Subjects:

Thirty obese females (with no other medical problems) were selected from the outpatient clinic of internal medicine in Kasr El-Aini hospital. Their ages ranged from 25-37 years & their BMI ranged from 30-35 kg/m². The patients were randomly allocated (by mean of random numbers) into one of two equal groups; *group 1*: the exercise group which received aerobic exercise training for 4 months and *group 2*: the non-exercise group which maintained their ordinary life style. The training exercises were conducted in the out patient clinic of Faculty of Physical Therapy. Thirty

healthy non-obese females were selected as a control group. Their ages ranged from 26-36 years & their BMI ranged from 21-24.5 kg/m²

Equipment and measurements:

1. Commercial kits to measure the serum levels of complement proteins (C3 & C4)
2. Weight and height scale (Metro type-England) was used to measure the weight and height to calculate the BMI. BMI=weight in kg/height in m².
3. Treadmill (Enraf Nonium, Model display panel standard, NR 1475.801, Holland) was used for walking exercises.

Measurement of C3 & C4 and calculation of BMI were done before starting the study for the obese and non-obese and control subjects and repeated at the end of the study (after four months) for the obese subjects.

Procedure:

Group 1: (15 females) received exercise training on bicycles ergometer; 3 sessions weekly, each session started with 5 minutes of aerobic exercise in the form of stretching exercise and walking in place (warm-up). Then the subject started the bicycle ergometer training for 40 minutes with an intensity of 65% of maximal heart rate for one

month and increased gradually to 85% of maximal heart rate during the next three months of the program. The workload is gradually reduced over 5 minutes (cool down).

Group 2: (15 females) asked to maintain their ordinary life style.

Statistical analysis:

Data were summarized using the mean (\pm SD). "t" test was used for comparisons between the mean values of C3 & C4 of the complement system and BMI in obese and control subjects and comparisons between the mean values of C3 & C4 of the complement system and BMI obtained before and after 4 months in the non-exercised and exercise group. Pearson's correlation test was used for correlation between BMI & complement "C3". P value is significant if < 0.05 .

RESULTS

Table (1) and figure (1) show comparison between non-obese (control) and obese subjects. There was no significant difference as regards the age. There were significant increase in the levels of C3 & C4 and BMI in obese compared to non-obese subjects.

Table (1): Comparison between control & obese subjects as regards age, BMI, C3 & C4

| Variables | Non-obese (control group) N=30 Mean (\pm SD) | Obese subjects N=30 Mean (\pm SD) | P value |
|---------------------------|---|--|---------|
| Age (years) | 30.4 \pm 3.86 | 28.9 \pm 5.78 | 0.24 |
| BMI (kg/m ²) | 22.87 \pm 1.1 | 33.52 \pm 2.2 | 0.001* |
| C3 (mg/dl) | 115.57 \pm 23.3 | 179.83 \pm 8.69 | 0.001* |
| C4 (mg/dl) | 19.67 \pm 6.9 | 40.03 \pm 1.87 | 0.001* |

C3= complement 3 C4= complement 4 BMI=body mass index *= significant

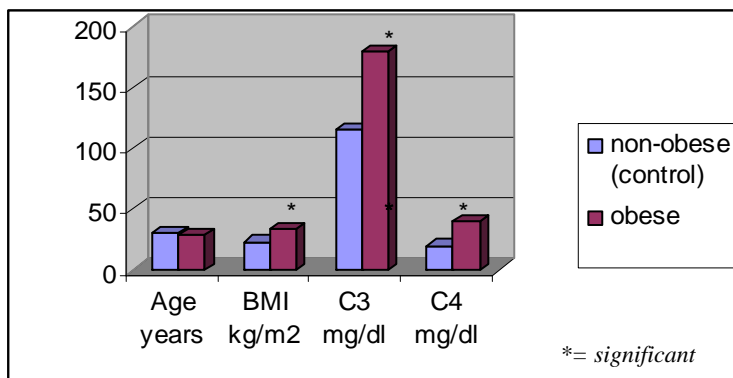


Fig. (1): shows significant differences in BMI, C3 & C4 between control & obese subjects

Table (2): Correlation between BMI and both C3 & C4 in obese subjects

| Parameter | BMI | |
|------------|------|---------|
| | r | P value |
| C3 (mg/dl) | 0.52 | 0.006* |
| C4 (mg/dl) | 0.32 | 0.04* |

*=significant

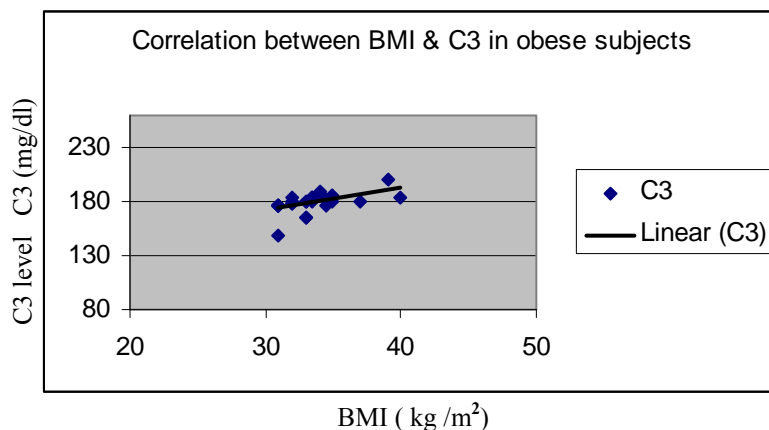


Figure (2) shows positive correlation between BMI & C3 in obese subjects

Table (3) and figure (3) show the differences between the C3, C4 levels & BMI at the start and the end of the study in the exercise group (group 1). There were significant

decreases in the mean values of C3, C4 & BMI in group (1) after the four months training exercise program. P value < 0.05.

Table (3): comparison between the start & the end values of C3, C4 & BMI in obese exercised group (1)

| Variables | Mean ± SD | | P value |
|---------------------------|--------------|---------------|---------|
| | At the start | At the end | |
| C3 (mg/dl) | 178.3 ± 9.87 | 133.4 ± 14.02 | 0.000* |
| C4 (mg/dl) | 39.4 ± 1.68 | 31.47 ± 5.1 | 0.000* |
| BMI (kg/m ²) | 32.96± 1.3 | 27.33 ± 1.87 | 0.000* |

C3= complement 3 C4= complement 4 BMI=body mass index *= significant

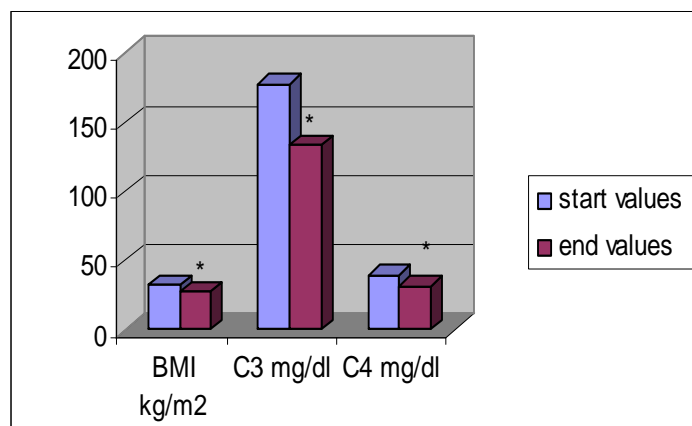


Fig. (3): Comparison between the start & end values of C3, C4 & BMI in group (1). The differences between the start and end values of C3, C4 & BMI in the non-exercise group (group 2) were shown in table (4) and figure (4). There were no significant differences between the pre and post measures. P-value > 0.05

Table (4): comparison between the start & the end values of C3, C4 & BMI in obese non exercised (group 2)

| Variables | Mean ± SD | | P value |
|---------------------------|--------------|---------------|-----------|
| | At the start | At the end | |
| C3 (mg/dl) | 181.4 ± 7.34 | 186.8 ± 13.36 | 0.25 (NS) |
| C4 (mg/dl) | 40.6 ± 1.92 | 38.13 ± 5.76 | 0.16 (NS) |
| BMI (kg/m ²) | 34.08± 2.77 | 34.25± 4.4 | 0.89 (NS) |

NS= non significant

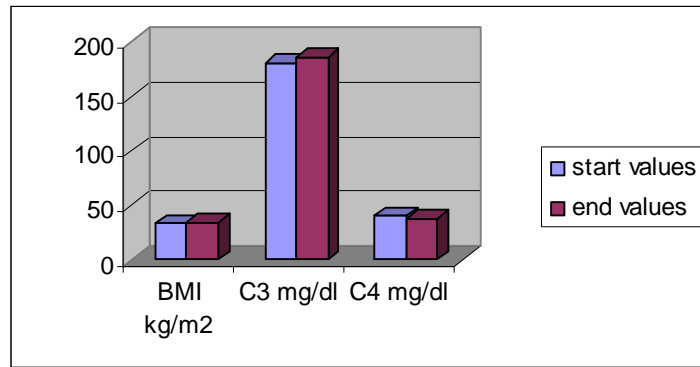


Fig. (4): Shows no significant differences between the start & the end values of C3, C4 & BMI in group (2)

Comparison between group (1) & group (2) at the start of the study revealed no significant differences as

regards BMI, C3 & C4 (table 5) & (figure 5).

Table (5): Comparison between group (1) & group (2) as regards C3, C4 & BMI at the start of the study:

| Variables | Means ±SD | | P value |
|--------------------------|-------------------|------------------------|-----------|
| | Exercise group(1) | Non-exercise group (2) | |
| C3 (mg/dl) | 178.3 ± 9.87 | 181.4 ± 7.34 | 0.1 (NS) |
| C4 (mg/dl) | 39.4 ± 1.68 | 40.6 ± 1.92 | 0.28 (NS) |
| MBI (kg/m ²) | 32.96± 1.3 | 34.08± 2.77 | 0.1 (NS) |

NS= non significant C3= complement 3 C4= complement BMI=body mass index

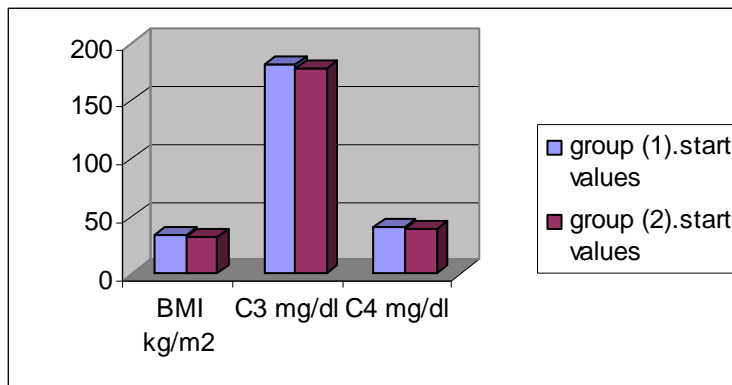


Fig. (5) Shows no significant differences between group 1 & 2 as regards BMI, C3 & C4 at the start of study

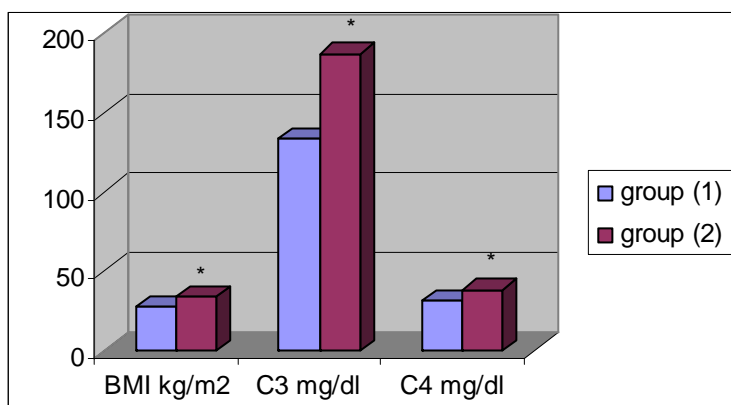
Comparison between obese exercised group (1) & obese nonexercised group (2) at the end of the study revealed significant differences as regards BMI, C3 & C4

(table 6) & (figure 6). There were significant decrease in BMI, C3 & C4 in the exercise group compared to non-exercise group (P-value<0.05).

Table (6): comparison between group (1) & group (2) as regards C3, C4 & BMI at the end of the study:

| Variables | Mean ± SD | | P value |
|---------------------------|-------------------|-------------------|---------|
| | Exercise group(1) | Control group (2) | |
| C3 (mg/dl) | 133.4 ± 14.02 | 186.8 ± 13.36 | 0.000* |
| C4 (mg/dl) | 31.47 ± 5.1 | 38.13 ± 5.76 | 0.000* |
| BMI (kg/m ²) | 27.33 ± 1.87 | 34.25± 4.4 | 0.002* |

*= significant



* = significant

Fig. (6) Shows significant differences between groups 1 & 2 as regards BMI, C3 & C4 at the end of the study

DISCUSSION

Complement is a group of serum proteins which work with antibody activity to eliminate pathogens. Complement stimulates inflammation, facilitates antigen phagocytosis, and lyses some cells directly. Because it is

such a powerful inflammatory agent, its activity is tightly regulated. Complement C3 and C4 are the major plasma proteins of the immune system complement pathways³.

Total body fat seems to be associated with a chronic low-grade systemic inflammation in apparently healthy adolescents. Central obesity is

independently associated with high C3 concentrations. The strong relations of body fat with C3 and C4 levels suggested that this increase could be due to an increased production in adipocytes, apart from other complement-producing tissues (i.e. hepatic cells, fibroblast, mononuclear cells, and endothelial cells^{9,12}).

In the present study, there were significant increases in the levels of both complement proteins C3 & C4 in obese compared to non-obese female and these increases in complement proteins correlated with the degree of obesity as represented by the body mass index (BMI). This agrees with previous studies^{9,13,14}. Obese adults have higher C3 concentrations compared to control subjects^{13,14}. Both C3 and C4 have shown substantial correlations with obesity, and high gene expression of these complement components has been reported in omental adipose tissue in obese subjects⁹.

Both C3 and C4 have been related to complications of obesity in adults¹⁵⁻¹⁷. Activation of the complement system may play a role in the development of macro vascular disease in type II diabetes¹⁸.

Exercise has been widely believed to be a preventive and therapeutic aid in the treatment of various pathophysiological conditions such as cardiovascular disease and cancer¹¹. Recent studies have shown that there are physiological changes in the immune system as a response to exercise. During moderate exercise immune cells circulate through the body more quickly and are better able to kill bacteria and viruses and exercise stimulates macrophage

function. After exercise, the immune system activity generally returns to normal within a few hours, but consistent, regular exercise seems to make these changes a bit more long-lasting. When moderate exercise is repeated on a near-daily basis there is a cumulative effect that leads to a long-term immune response. However, there is also evidence that too much intense exercise can reduce immunity. Intense exercise seems to cause a temporary decrease in immune system function. Research has found that during intense physical exertion, the body produces certain hormones (Cortisol and adrenaline) that temporarily lower immunity¹⁹.

In the present study, a group of obese females were subjected to moderate aerobic exercise training three sessions weekly for 4 months and another group of obese females were not subjected to exercise and maintained their ordinary life style. There was a significant weight reduction in the exercise group after the 4 months with decrease of BMI from 32.96 ± 1.3 to 27.33 ± 1.87 kg/m² ($P < 0.00$), while the obese nonexercised group showed no significant changes in body weight after the 4 months. This agrees with the previous studies which support the role of exercise in weight reduction in obese subjects²⁰⁻²³. Some authors explained the effect of exercise on weight reduction by increasing fat oxidation in muscles²¹, others explained that by increasing energy expenditure^{22,23} and some explained that by changes in appetite by the effect of certain hormones²⁰.

In the present study, there was a significant reduction in the serum

levels of complement component C3 & C4 in the exercise group with no significant changes in the obese nonexercised group after the 4 months. This is supported by the previous findings that serum levels of C3 were higher in obese subjects than in controls and were decreased after weight loss. Also, changes in serum levels of the classical pathway components C1q, C2, and C4 are correlated with change in body weight in both obese women and those who lost weight due to anorexia^{14,24}. Serum C4 levels in both genders correlated with visceral fat area, with high levels of C4 transcripts detected in omental adipose tissue⁹. Acylation stimulating protein (ASP) which is a precursor of complement component 3 (C₃) become higher in obese subjects. Obese humans have 58-400% increase in (ASP) above normal. Four week fast and exercise resulted in reduction of (ASP) to normal levels in these obese subjects. Weight loss has been shown to decrease ASP levels which decrease atherosclerosis, also plasma C3 decrease with weight loss²⁵.

So, in the present study, it was found that a program of moderate intensity exercise for weight reduction, three sessions / week for 4 months lead to significant changes in immune system in the form of the significant reduction of C₃ & C4 serum levels. This beneficial effect of moderate exercise on the immune system could be related to the significant weight reduction produced by exercise or might be due to direct effect of moderate exercise on the immune system

As there is a dual effect of exercise on the immune system; moderate intensity exercise lowers the incidence of infections while intense exercise increases it. Several studies investigated the underlying mechanisms of such a relationship. Two principal research approaches have emerged in trying to establish a link between exercise and the immune system a metabolic approach that involves glutamine metabolism and another that considers changes in the neuroendocrine milieu as the mechanism for immunomodulation¹⁹.

Conclusion: obesity causes changes in the immune system in the form of increase in C3 & C4 levels. Moderate aerobic exercise produced significant weight reduction in obese females and decreased the abnormally elevated complement components (C3 & C4); so improving the immune system.

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إستجابة الجهاز المناعي للتمرينات الرياضية في السيدات البدنيات

هدف هذا البحث هو دراسة تأثير التمرينات الرياضية العلاجية على الجهاز المناعي عند السيدات البدنيات وذلك عن طريق دراسة إستجابة العامل المناعي المكمل للتمرينات الرياضية. أجرى هذا البحث على ثلاثين سيدة تعاني من البدانة تتراوح أعمارهم من خمس وعشرون إلى سبع وثلاثون سنة مقسمين إلى مجموعتين متساويتين في العدد:

المجموعة الأولى (أ) خضعت للتمرينات الرياضية. ولقد تمت ممارسة برنامج التمرينات في فترة ٤ شهور بمعدل ٣ مرات أسبوعياً ومدة الجلسة تصل إلى ساعة كاملة
والمجموعة الثانية (ب) وهي المجموعة التي لم تخضع للتمرينات والمجموعة الخاكمة وتشمل ثلاثين من السيدات غير البدنيات

نتائج البحث:

أظهرت النتائج تحسن ملحوظ في الجهاز المناعي المكمل بعد فقدان هؤلاء السيدات معظم الوزن الزائد في الجسم وأدى ذلك إلى انخفاض نسبة العامل المناعي المكمل (C3&C4) ومن ثم أدى هذا الانخفاض إلى تحسن الجهاز المناعي لهؤلاء السيدات اللاتي اشتركن في برنامج التمرينات ولم يحدث تحسن في المجموعة البدنية التي لم تخضع للتمرينات.
ونستخلص من هذا البحث ضرورة المحافظة على الوزن المثالي ومتابعة التمرينات الرياضية للتخلص من أي وزن زائد كي نتحاشى الأمراض المختلفة الناتجة عن السمنة ومن أهمها التأثيرات السلبية للسمنة على الجهاز المناعي للجسم وعلى صحة الإنسان.