

# Immune System Response to Weight Loss among Obese Saudi Non-Alcoholic Fatty Liver Disease Subjects

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## Abstract

**Background:** Globally, non-alcoholic fatty liver disease (NAFLD) is medical problem. Obesity is related to NAFLD. However, obesity has been linked to dysfunctional immune system.

**Objective:** The main target of this study was to measure the immunological parameters after weight loss among NAFLD obese Saudi subjects.

**Material and Methods:** Ninety obese Saudi individuals with NAFLD enrolled in our study, the range of the participants' age was 42-53 years, where the range of BMI was 32-36 kg/m<sup>2</sup>. Participants were randomly assigned in group (A) received weight reducing program for 3 months, where group (B) received no intervention.

**Results:** There was a 32.7%, 31.8%, 32.1%, 21.9%, 33.7%, 6%, 12% and 24.3% reduced mean values of BMI, WBCs, monocytes, total neutrophil count, CD3, CD4, CD8 and CD4/CD8 ratio in group (A) respectively. While, there was a 3.5%, 3.3%, 4.9%, 2.9%, 3.7%, 2.5%, 3.6%, and 3.4% increased mean values of the same variables of group (B). Moreover, at the end of the study both groups revealed significant differences.

**Conclusion:** Weight loss improves immunological parameters among obese NAFLD subjects.

**Keywords:** Immune system; Non-alcoholic fatty liver disease; Obesity; Weight loss

## Introduction

Globally, non-alcoholic fatty liver disease (NAFLD) considered as a common chronic liver disorder [1]. Similarly, about 30% of European people have NAFLD [2]. Moreover, about 25-50% of worldwide people have NAFLD which is the major cause of abnormal liver enzymes [3]. There is an association between NAFLD and obesity [4]. Abnormal immunological and systemic inflammation parameters are the key for NAFLD pathogenesis [5-8]. However, abnormal immune system performance not only induce NAFLD but also contributes progression and NAFLD associated disorders [9-11]. In addition, obesity is usually associated with abnormal immunological parameters values [12]. Altered immune system competence is usually a common finding associated with obesity subjects and the level of deterioration in immune system performance is related to obesity grade [13]. Similarly, about 30% of some malignant tumors are associated with obesity [14]. Many researchers reported abnormal values of immune system parameters among obese individuals [15-17].

Till now, there is no pharmacy approved for NAFLD worldwide [18,19]. However, life style intervention is the considered management for NAFLD [20], which include control of diet and physical exercise to induce weight loss, while some evidence considered a 7% body weight loss as a minimum accepted level to improve liver function of NAFLD subjects [21]. Limited evidences are available regarding immune system response to weight loss among NAFLD subjects, so that the main target of our trail was to detect the effect of weight loss on immunological parameters among NAFLD individuals.

## Patients and Methods

### Subjects

Ninety obese Saudi individuals with NAFLD enrolled in our study, the range of the participants' age was 42-53 years, where the range of BMI was 32-36 kg/m<sup>2</sup>, were selected from patients of Internal Medicine Department in Teaching hospital of King Abdulaziz University. Diagnosis of NAFLD was confirmed by ultrasonography findings [22,23]. Patients with hypertension, alcohol consumption, cigarette smoking, corticosteroids, pregnancy, malignancy, diabetes, thyroid disorders, hepatitis B, hepatitis C and liver cirrhosis were excluded from the study. Participants were randomly assigned in group (A) received weight reducing program for 12 weeks, while group (B) asked to stay at their regular life style without therapeutic intervention. A consent form was signed by participants before sharing in our study that was ethically approved by FAMS Ethical Research Committee, King Abdulaziz University.

### Measurements

**Analysis of peripheral blood cells:** Beckman Coulter AcT 5diff hematology analyzer was used for analysis of peripheral blood cells.

**Flow cytometry analysis:** Leukocyte differentiation antigens CD3, CD4 and CD8 were measured using Beckman Coulter, Marseille, France. However, flow cytometry (Cytomics FC 500 and CXP software was used for analysis of samples.

### Procedures

Participants were randomly assigned in 2 groups as following:

A. Group (A) received weight reducing program for three months which include treadmill (Enraf Nonium, Model display panel Standard, NR 1475.801, Holand) aerobic exercise training that aligned with the American College of Sports Medicine recommendations [24]. Program of training consisted of warming up for five minute, half an hour of training at intensity equal 60-70% maximum heart rate of each individual followed by ten minutes cooling down , three sessions /week

for 12 weeks . In addition, diet control under supervision of an experienced dietician to limit calorie control to 1200 Kilo Calorie every day for 12 weeks [25-27].

B. Group (B) asked to stay at their regular life style without therapeutic intervention.

### Results

Demographic variables of all participants proved that both groups were homogeneous as comparison between the both groups regarding demographic and baseline variables showed no significant differences (Table 1). There was a 32.7%, 31.8%, 32.1%, 21.9%, 33.7%, 6%, 12% and 24.3% reduced mean values of BMI, white blood cells, total neutrophil count, monocytes, CD3, CD4, CD8 and CD4/CD8 ratio in group (A) (Table 2) respectively. While, there was a 3.5%, 3.3%, 4.9%, 2.9%, 3.7%, 2.5%, 3.6%, and 3.4% increased mean values of the same variables of group (B) (Table 3). Moreover, at the end of the study both groups revealed significant differences (Table 4).

**Table 1:** Participants baseline criteria.

	Mean +SD	
	Group (A)	Group (B)
Age (year)	45.39±5.58	43.81±4.92
Gender (F/M)	24/21	23/22
BMI (kg/m <sup>2</sup> )	31.98±2.64	31.16±2.95
AST (IU)	66.26±8.15	64.75±6.74
ALT (IU)	54.17±5.24	53.46±4.85
AST/ALT	1.21±0.82	1.19±0.76
Fasting glucose(mg/dl)	151.62±14.19	148.37±12.58
Insulin (mU/l)	15.31±2.74	13.88±2.93
SBP (mmHg)	133.12±12.67	130.87±10.52
DBP (mmHg)	82.35±5.11	81.61±4.23

BMI: Body Mass Index; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; AST/ALT: Aspartate Aminotransferase/Alanine Aminotransferase Ratio; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure.

**Table 2:** Statistical analysis of group (A) variables.

	Mean + SD		t- value	Significance
	Pre	Post		
BMI (kg/m <sup>2</sup> )	31.98±2.64	27.65±2.43*	6.12	P <0.05
White blood cells count (10 <sup>9</sup> /μL)	9.35±1.78	7.29±1.54*	6.83	P<0.05
Total neutrophil count (10 <sup>9</sup> /μL)	5.32±1.31	3.56±1.12*	5.78	P<0.05
Monocytes (10 <sup>9</sup> /μL)	0.74±0.25	0.51±0.13*	4.67	P<0.05
CD3 cell count (10 <sup>9</sup> /L)	1.88±0.63	1.43±0.51*	5.19	P<0.05
CD4 cell count (10 <sup>9</sup> /L)	1.51±0.61	1.27±0.55*	5.28	P <0.05
CD8 cell count (10 <sup>9</sup> /L)	0.89±0.32	0.56±0.21*	4.73	P <0.05
CD4/CD8 ratio	1.48±0.85	1.13±0.76*	5.64	P <0.05

BMI: Body Mass Index; (\*) indicates a significant difference between the two groups, P < 0.05.

**Table 3:** Statistical analysis of group (B) variables.

	Mean + SD		t- value	Significance
	Pre	Post		
BMI (kg/m <sup>2</sup> )	31.16±2.95	31.67±2.59	0.78	P>0.05
white blood cells count (10 <sup>9</sup> /μL)	9.18±1.69	9.42±1.71	0.92	P>0.05
total neutrophil count (10 <sup>9</sup> /μL)	5.44±1.52	5.51±1.53	0.86	P>0.05
Monocytes (10 <sup>9</sup> /μL)	0.78±0.19	0.83±0.20	0.65	P>0.05
CD3 count (10 <sup>9</sup> /L)	1.91±0.66	1.96±0.67	0.81	P>0.05
CD4 count (10 <sup>9</sup> /L)	1.55±0.58	1.61±0.62	0.73	P>0.05
CD8 count (10 <sup>9</sup> /L)	0.93±0.29	0.97±0.31	0.88	P>0.05
CD4/CD8 ratio	1.62±0.53	1.65±0.52	0.65	P>0.05

BMI: Body Mass Index;

**Table 4:** Statistical analysis of group (A) and group (B) variables at the end of the study.

	Mean + SD		t- value	Significance
	Group (A)	Group (B)		
BMI (kg/m <sup>2</sup> )	27.65±2.43*	31.67±2.59	6.14	P <0.05
white blood cells count (10 <sup>9</sup> /μL)	7.29±1.54*	9.42±1.71	5.72	P<0.05
total neutrophil count (10 <sup>9</sup> /μL)	3.56±1.12*	5.51±1.53	5.64	P<0.05
Monocytes (10 <sup>9</sup> /μL)	0.51±0.13*	0.83±0.20	4.25	P<0.05
CD3 count (10 <sup>9</sup> /L)	1.43±0.61*	1.96±0.67	4.83	P <0.05
CD4 count (10 <sup>9</sup> /L)	1.27±0.75*	1.61±0.62	4.21	P <0.05
CD8 count (10 <sup>9</sup> /L)	0.52±0.21*	0.97±0.31	4.17	P <0.05
CD4/CD8 ratio	1.13±0.76*	1.65±0.52	4.31	P <0.05

BMI: Body Mass Index; (\*) indicates a significant difference between the two groups, P < 0.05.

**Discussion**

Globally, up to 90% of obese patients have NAFLD [28]. While, obesity has been linked to dysfunctional immune system [29]. However, poor function of immune system involved in fatty liver pathophysiological [9,10]. Moreover, we have no standard treatment for NAFLD, rather than reducing body weight [30]. For the best of what we know, limited evidences are available regarding immune system response to weight loss among NAFLD subjects, so that the main target of this study was to measure the immunological parameters response to weight loss among NAFLD obese Saudi subjects. The present study findings aligned with Shade et al. [31] reported that among 114 postmenopausal women who shared in an exercise program and had greater than ten pounds loss in their body weight resulted in lower level of natural killer cell (NK) cytotoxicity which indicates improved immune system function associated with weight reduction [31]. However, Wasinski et al. [32] proved that weight reducing program on mice which included about 30% restriction in caloric intake in addition to five sessions/ weekly of swimming training for 6 weeks resulted in reduced values of CD4+ and CD8+ T lymphocytes [32]. Also, Carpenter et al. [33] mentioned that exercise training for two months improved immunological parameters of diet-induced obese associated with weight loss [33].

Viardot et al. [34] found in their study on thirteen non-insulin dependent diabetic obese subjects who had a diet control for 24 weeks in addition to gastric banding at the 12th week, their results revealed reduced values of pro-inflammatory T-helper cells, monocytes and neutrophils as result of weight loss [34]. While, Wing et al. [35] stated that after two weeks of fasting, improvement in NK cell cytotoxic activity and monocytes bactericidal capacity as a result of weight loss [35]. Moreover, Tanaka et al. [36] reported that T cell counts & NK cell activity improved following caloric restriction [36]. Similarly, Zhang et al. [37] recorded improvement in circulating immunoglobulins, glucose control and blood lipid profile following laparoscopic sleeve gastrectomy in 48 obese patients [37]. Improved immune system parameters following weight reducing program may be due to reduced adipose tissue mass, serum levels of inflammatory cytokines and leptin in addition to improved insulin sensitivity [38-41].

**Conclusion**

Life style modification improves immunological parameters among obese NAFLD subjects.

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