Comparison of Inflammation on Obese Individuals and Patients Diagnosed with Type 2 Diabetes Mellitus

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Abstract: Obesity is expressed as increased body fat tissue mass. Obesity is the most frequent cause of insulin resistance. Insulin resistance leads to formation of type 2 diabetes mellitus within a period of 10-15 years. Due to this mechanism, there is a strong relationship between obesity and type 2 diabetes mellitus. This study aimed to compare obesity and type 2 diabetes mellitus, which occur with similar mechanisms, based on the inflammation they cause. Ninety-seven male and female individuals were included in the study. The participants were divided into three groups as the control group (n=31), obese group (n=33) and type 2 diabetes group (n=33). Their clinic biochemical tests were obtained retrospectively from their files and analyzed. The Neutrophil / Lymphocyte (N/L) ratios of the control, obese non-diabetic and type 2 diabetes mellitus groups were found respectively as (mean±SD) 1.76 ± 0.69, 1.95 ± 0.89 and 2.79 ± 2.16 (p=0.01). While N/L was numerically higher in the obese non-diabetic group in comparison to the control group, the difference was not statistically significant (p>0.05). This value was found to be significantly higher in the type 2 diabetes mellitus group than the other two groups (p<0.05). It is seen that type 2 diabetes mellitus development in obese non-diabetic individuals may be prevented by weight loss as a result of lifestyle changes, healthy and balanced diet, exercise and increased mobility, and this way, progression of systemic inflammation and formation of tissue and organ damage may be counteracted. In addition, if the transformation of insulin resistance into type 2 diabetes mellitus in obese individuals can be prevented, cardiovascular morbidity and mortality may decrease.

INTRODUCTION

Obesity is expressed as increased body fat tissue mass. Disruption of the balance between the obtained and spent energy and a continuous increase in fat tissue as energy storage as a result of higher levels of energy intake are at the basis of obesity. The prevalence of obesity is increasing very fast in the World and in Turkey. Moreover, the initial onset of obesity has gradually decreased down to the childhood period. Obesity is a highly significant and very high-cost health issue with its direct and indirect effects. The main indirect effects of obesity can be listed as increased prevalence of hypertension, glucose metabolism disorders, atherosclerosis, heart diseases and some cancers. These diseases are also the most common causes of death. As it is difficult to directly measure the fat tissue in the body, methods that show the amount of fat tissue indirectly are used in the diagnosis of obesity. The main one among these methods is the body mass index (BMI). BMI calculation is calculated by dividing weight to height square. BMI value can be obtained easily after height and weight measurements are made. In addition to this, as an indicator of obesity, calculations such as waist circumference and the ratio of waist circumference to hip circumference may be made. The excessive increase in fat tissue in obesity is not only a visual and physical problem. In addition to the functions of adipose tissue known so far such as achievement of heat balance, energy storage and storage of fat-soluble vitamins, it has autocrine, paracrine and endocrine effects that have been recently understood. It has been understood that about 20 hormones and cytokines that are known as adipocytokines and secreted from fat tissue are significant factors in inflammation, insulin resistance and metabolic syndrome processes. The main adipocytokines may be listed as leptin, adiponectin, resistin, visfatin, apelin, ghrelin, obestatin, omentin, adipsin, lipoprotein lipase, TNF alpha and Interleukin-6-8-10-18. A part of these adipocytokines trigger inflammation[1-5]. Obesity is the most frequent cause of insulin resistance. Insulin resistance refers to the inability of insulin to be effective due to problems at the pre-receptor, receptor or post-receptor stage despite normal or excess concentration of insulin in circulation. If insulin resistance cannot be alleviated by lifestyle change, natural, balanced and healthy nutrition, exercise and a more active lifestyle or small and mild calory intake restriction, it leads to formation of type 2 diabetes mellitus (DM) within a period of 10-15 years. Type 2 DM is a chronic disease with many severe complications. Due to this mechanism, there is a

strong relationship between obesity and type 2 DM[6]. The fasting plasma glucose concentration is kept constant between 70 and 100 mg/dl. If the fasting plasma glucose concentration has exceeded 126 mg/dl due to various metabolic disorders, the diagnosis of DM is made. Type 2 DM is the most prevalent type of DM (90%). It develops as a result of the insulin resistance mechanism. Therefore, it is closely related to obesity. The increases in the prevalence of obesity and type 2 DM show parallelism. Type 2 DM has several chronic complications. Its main complication may be disseminated tissue inflammation[7-9]. The ratio of the numbers of neutrophils to lymphocytes (N/L) is used as an indication of systemic inflammation[10]. This study aimed to compare obesity and type 2 DM, which occur with similar mechanisms, based on the inflammation they cause.

MATERIALS and METHODS

Ethical approval

The study was conducted with the approval of the Clinical Studies Ethics Board of Alanya Alaaddin Keykubat University (ALKU-KAEK) with the decision dated 17.01.2019 and numbered 2019/1. Research was carried out in compliance with the ethical principles of the Declaration of Helsinki accepted in 1964 by the World Medical Association and has been continuously revised since.

Study design

Ninety-seven male and female individuals in the age range of 44-75 who visited the Alanya Research and Training Hospital of Alanya Alaaddin Keykubat University were included in the study by obtaining their consents. The participants were divided into three groups as the control group with 31 individuals (15 women, 16 men) (in the normal body mass index range), 33 obese individuals without diagnosis of type 2 DM and any other chronic diseases (19 women, 14 men) (obese non diabetic) and 33 type 2 diabetes patients (20 women, 13 men). The patients signed a voluntary consent form. Their routine tests were obtained retrospectively from their files and analyzed.

Statistical analysis

The data that were obtained were subjected to statistical analysis. Using the SPSS software, ANOVA was applied. Post-hoc tests were applied to understand the source of the significant differences among the groups. The level of significance in the comparisons among the groups was accepted as $p<0.05$.

RESULTS

The Neutrophil/Lymphocyte (N/L) ratios of the control, obese non-diabetic and type 2 DM groups were found respectively as (mean±SD) 1.76 ± 0.69, 1.95 ± 0.89 and 2.79 ± 2.16 (p=0.01). When the Tukey HSD test was applied to find the source of the difference, although the N / L was higher in the obese non-diabetic group compared to the control group, the difference was not statistically significant. (p>0.05). This value was found to be higher in the type 2 DM group than the other two groups (p= (respectively) 0.013, 0.047). Table 1 shows the comparisons of all clinical biochemical parameters among the groups, below.

Table 1. Biochemical parameters in obese individuals and patients diagnosed with type 2 diabetes

Parameter	Control group (n=31) (Mean±SD)	Obese Nondiabetic (n=33) (Mean±SD)	Type 2 Diabetes Mellitus (n=33) (Mean±SD)	p
Glucose	96.65 ± 14.37	97.61 ± 12.58	164.30 ± 56.43 * #	<0.001
HbA1C (%)	5.55 ± 0.46	5.66 ± 0.45	7.83 ± 1.08 * #	<0.001
AST	20.35 ± 6.26	19.06 ± 7.12	20.09 ± 11.67	0.82
ALT	22.94 ± 14.08	23.18 ± 13.19	28.27 ± 21.93	0.36
BUN	30.65 ± 8.89	30.24 ± 9.41	33.18 ± 11.28	0.43
Creatinine	0.83 ± 0.14	0.78 ± 0.14	0.87 ± 0.16 #	0.04
Hemoglobin	13.39 ± 1.52	13.86 ± 1.94	13.29 ± 1.61	0.22
Neutrophils	3.74 ± 1.17	4.08 ± 1.34	4.91 ± 1.43 * #	0.002
Lymphocytes	2.25 ± 0.79	2.32 ± 1.12	2.14 ± 0.69	0.71
Neutrophils / Lymphocytes	1.76 ± 0.69	1.95 ± 0.89	2.79 ± 2.16 * #	0.01
Body Weight (Kg)	71.90 ± 13.13	88.67 ± 12.63 *	87.18 ± 15.42 *	<0.001
Height (cm)	165.94 ± 11.17	160.58 ± 10.20	159.09 ± 11.04 *	0.34
Body Mass Index	23.97 ± 3.41	34.41 ± 4.36 *	34.69 ± 6.64 *	<0.001

*: Statistically significant difference in comparison to the control group, #: Statistically significant difference in comparison to the obese non-diabetic group (p<0.05).
(By Anova and post-hoc Tukey HSD analyses).

DISCUSSION

The Neutrophil/Lymphocyte ratio (N/L) is used as an inexpensive, practical and good indicator of systemic inflammatory response[10, 11]. The prevalence of obesity is increasingly higher in the society. The most frequent cause of insulin resistance is obesity. After formation of insulin resistance, this may lead to formation of Type 2 DM within 15 years[7]. For these reasons, obesity may be considered as a preliminary condition for type 2 DM. Our study compared the N/L ratios as an indicator of possible systemic inflammatory response that occurs in cases of obesity and type 2 DM. Although the N/L ratio was numerically higher among the obese individuals in comparison to the control group, the increase was not significant (p>0.05). In the type 2 DM group, the N/L ratio was higher than that of the control group (p=0.01). Similar studies in the literature showed a significant increase in the N/L ratio after development of insulin resistance[12]. The N/L ratio may reach a significant level by making a comparison among higher numbers of obese and total participants in studies or larger samples. Additionally, looking at the HOMA-IR index for insulin resistance measurement as a selection criterion for the obese group whose N/L ratio is to be examined and selecting those diagnosed with insulin resistance will allow better observation of inflammation

development. Obesity is accepted as a chronic disease, and it is recommended to be treated even if there are no other accompanying diseases. While obesity causes several metabolic disorders, it also increases systemic inflammation and may as a result lead to function disorders and damage on the tissue and organ levels[12, 13]. The ALT levels in the obese non-diabetic group and the type 2 DM group were higher in comparison to the control group, but the difference was not significant (p>0.05). The creatinine levels in the type 2 DM group were higher than the obese non-diabetic group (p=0.04). If insulin resistance followed by type 2 DM develops in obese individuals, kidney functions are affected negatively. In the comparison of the number of neutrophils in the groups, similar results were observed to those on the N/L ratio. While the number of neutrophils was numerically higher in the obese individuals than the control group, the increase was not significant (p>0.05). The neutrophil numbers in the type 2 DM group were significantly higher than those in the control patients (p=0.02). Considering in terms of the body mass index (BMI), the mean value was 34.41 ± 4.36 in the obese non-diabetic patients and 34.69 ± 6.64 in the type 2 DM patients (p>0.05). The finding that there was a difference between the obese non-diabetic patients and the type 2 DM patients in terms of N/L despite the absence of a difference in terms of BMI showed that systemic inflammation probably developed not only by an increase in BMI but also by development of insulin resistance and type 2 DM later. It is seen that type 2 DM development in obese non-diabetic individuals may be prevented by weight loss as a result of lifestyle changes, healthy and balance diet, exercise and increased mobility, and this way, progression of systemic inflammation and formation of tissue and organ damage may be counteracted. While obesity increased systemic inflammation in the case of no other accompanying chronic diseases, this difference was not found significant (p>0.05). There was a difference in the type 2 DM patients in comparison to both the obesity group and the control group (p<0.05). Obesity triggers the inflammation process. If obesity continues for a long term accompanied by insulin resistance, a more noticeable inflammation process occurs following development of type 2 DM. While type 2 DM development may be prevented by treatment and alleviation of insulin resistance with weight loss and lifestyle changes, it may also be possible to prevent progression of inflammation. This way, damage formation in tissues and organs may be prevented. It is clear from studies conducted in the literature to date that there is a significant relationship between cardiovascular morbidity, mortality and NLR[14-17]. The NLR was significantly elevated in patients with low HDL-C when compared with control participants in a clinical study[14]. Thus, high NLR values can disrupt cholesterol metabolism. Another study showed that NLR was associated with the development of AF in patients presenting ST-elevated myocardial infarction (STEMI)[15]. Therefore, high NLR values may adversely affect the course of STEMI. Another study in the literature demonstrated that NLR was significantly elevated in patients with mitral annular calcification (MAC) and it was correlated with MAC[16]. Due to the relationship between MAC and coronary artery diseases, high NLR values may lead to cardiovascular diseases. In another study, it was demonstrated that there was a predictive value of inflammation markers in new-onset atrial fibrillation after coronary artery bypass grafting[17]. NLR can be a predictor of cardiovascular outcomes and that cardiovascular mortality and morbidity may be higher in diabetic and obese patients. Cardiovascular morbidity and mortality can be reduced in obese patients by reducing insulin resistance and preventing the development of type 2 diabetes.

Conclusion

It is seen that type 2 DM development in obese non-diabetic individuals may be prevented by weight loss as a result of lifestyle changes, healthy and balanced diet, exercise and increased mobility, and this way, progression of systemic inflammation and formation of tissue and organ damage may be counteracted. In addition, if the transformation of insulin resistance into type 2 diabetes mellitus in obese individuals can be prevented, cardiovascular morbidity and mortality may decrease.

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