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Research Article

METABOLIC SYNDROME, SKIN TAGS, LEPTIN AND LIFESTYLE CHANGE

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ABSTRACT

Most commonly, skin tags (STs) appear in middle-aged and elderly people's necks and axillae. Diabetes and cardiovascular disease are risk factors of metabolic syndrome (MS). There is a strong association between MS and hyperleptinaemia and leptin resistance in studies of different ethnic groups. The purpose of this study is to determine whether skin tags and leptin levels may be related to MS based on diagnostic criteria developed by the International Diabetes Federation (IDF). 80 participants were enrolled in this study, 40 of whom were ST patients and 40 of whom were apparently healthy controls. As well as triglycerides, cholesterol, HDL, criteria for MS, WC, BMI, fasting glucose levels, smoking status, insulin resistance, and insulin levels, all of these aspects were assessed. A univariate analysis revealed significant differences in WC, BMI, insulin resistance, fasting glucose, insulin levels, HDL, leptin levels, cholesterol and triglycerides between ST patients and controls (P 0.001). Among the MS components and ST, the multivariate analysis revealed only high triglyceride levels (OR 1.204/95% CI 1.043-1.392/P = 0.012) and low HDL levels (OR 0.553/95% CI 0.385-0.800/P = 0.003) were significantly associated with ST. High triglyceride levels were significantly associated with high plasma leptin levels when examining the predictors of high plasma leptin levels. The study indicates that ST patients may also have hyperleptinemia and high triglycerides, suggesting they may benefit from changing their lifestyle.

Keywords: - Skin Tags, hyperleptinemia, Leptin levels.

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INTRODUCTION

There are several alternative terms to describe soft fibromas, skin tags (STs), acrochordons or fibroepithelial polyps, which are benign growths of skin that protrude from surrounding skin [1]. Polypoid lesions are characterized by soft, slightly acanthotic epidermis, loose, mild chronic inflammation and oedematous fibrovascular core. [2] STs are associated with skin friction. [3] There is evidence that STs are associated with diabetes mellitus (DM) (type 2) and obesity [4-8]. There are numerous interrelated risk factors for cardiovascular disease (CVD) and diabetes (DM) in metabolic syndrome (MS). There are several factors responsible for these problems, including high blood pressure, high cholesterol levels diabetes, hypertriglycemia, low high-density lipoproteins (HDL), obesity (particularly central obesity) and high cholesterol levels [9]. In the body, leptin is synthesised primarily by adipocytes, while serum leptin levels are determined by serum levels of leptin [10]. Leptin contains 167 amino acids encoded by the ob gene. As adipocyte cell size increases, leptin secretion increases, and plasma leptin levels increase in proportion to fat mass [11]. Appetite is suppressed and energy expenditure is increased by the hormone leptin, [12] but it is also responsible for regulating energy reserves.

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According to multiple epidemiological studies of different ethnic groups [13], hyperleptinemia and resistance to leptin are strongly associated with multiple sclerosis and contribute significantly to cardiovascular mortality and morbidity [14]. Leptin may also contribute to ST pathogenesis, as an adipoimmune [15]. As guided by the International Diabetes Federation (IDF) diagnostic criteria, we aim to study the possible relationship between STs and leptin levels with MS.

METHODS

The present study comprised 80 participants: 40 patients seeking advice about STs and 40 apparently healthy people matched by age and gender. All participants provided informed consent before participating in the study. An extensive history of hypertension, diabetes, smoking, cholesterol abnormalities, and family history of ST was taken from all participants. Clinical examination of STs included the number, location, and color of STs, as well as acanthosis nigricans. In order to determine the WC and calculate the BMI, the following equation was used: BMI = weight (kg)/height (m^2). During a 5-minute sitting period, participants' blood pressure was averaged from two measurements. Diabetic patients were diagnosed according to WHO guidelines or were being treated with an anti-diabetic drug. On the day of enrolment, venous samples were taken from participants after they had fasted overnight. All participants were measured for fasting blood sugar using enzyme colorimetric methods (glucose oxidase method) [16], a plasma colorimetric test was used to measure cholesterol, triglycerides, and HDL, [17] plasma insulin was measured using an enzyme colorimetric test and IR was measured using HOMA [18] plasma leptin was measured via enzyme linked immunosorbent assay (ELISA). Based on the consensus definition of the International Diabetes Federation (IDF), MS parameters were estimated [19].

Statistical analysis

For statistical analysis, data were expressed as standard deviation (SD) + mean, percentage (%) and frequency (no. of cases). Using Student's t-test, quantitative variables were compared between the study groups. In order to compare categorical data, the Chi square test (c2) was used. For linear relationships, Pearson's correlation equation was used to calculate correlations between variables. MS and ST occurrence were studied using stepwise multivariate logistic regression analysis, whereas ST number and plasma leptin levels were examined using multivariate linear regression analysis. Statistical significance was defined as a $P < 0.05$. For all statistical computations, Microsoft Excel 2007 (Microsoft Corporation, New York, United States) was used along with SPSS version 15.

RESULTS

This analytical descriptive study included 40 patients with STs (15 males/25 females) with mean age 40.8 ± 11.45 and mean number of ST lesions 11.1 ± 12.8, 24 patients (60%) were found with flesh colored STs, nine patients (22.5%) showed pigmented STs, and seven patients (17.5%) presented with mixed type STs. There were also 40 controls (22 females and 18 males), whose average age was 41.1 years old. A univariate analysis of the data showed that patients was significantly more likely to have WC, BMI, fasting glucose, insulin, and IR than controls. ($P < 0.001$). Moreover, their cholesterol and triglyceride levels were significantly higher, and their HDL levels were significantly lower ($P < 0.001$). There was a significant relationship between MS and patients compared to controls ($P < 0.001$) In addition, the patients' leptin levels were significantly higher than those of the controls ($P < 0.001$) [Table 1]. As far as age, sex, smoking habits, diabetes, and hypertension were concerned, univariate analyses revealed no significant differences between patients and controls. [Table 1]. MS components with ST occurrence were analyzed using stepwise multivariate logistic regression, and only high triglycerides (OR 1.204/95% CI 1.045-1.393/P = 0.012) and low HDL levels (OR 0.553/95% CI 0.385-1.001/P = 0.003) were statistically significant. [Table 2]. No significant association was found between MS components and STs in the multivariate linear analysis [Table 3]. Neither the number of STs nor leptin levels were significantly correlated with each other ($r = -0.03$, $P = 0.856$). Multivariate linear analysis of the predictors of high plasma leptin levels also revealed a significant association with high triglyceride levels (OR 0.286/95% CI 0.411–3.55/P = 0.015) and low HDL levels (OR -0.403/95% CI -8.5 to -2.07/P = 0.003) [Table 4].

Table No. 1. Patients data

	Patients (n*= 40)	**Controls (n = 40)**	***P* value**
Age (years)	40.8 ± 11.45	40.3 ± 11.54	0.745
Sex (♂/♀) (*n*, %)	15/25 (37.5/62.5)	18/22 (44/55)	0.495
Waist circumference (cm) (mean ± SD†)	108.65 ± 13.65	92.85 ± 17.16	<0.001‡
BMI§ (mean ± SD)	34.3 ± 7.04	27.04 ± 4.27	<0.001‡
Smoking (*n*,%)	8 (21.4)	14 (33.4)	0.316
Diabetes (*n*,%)	4 (12.4)	3 (6)	0.236
Hypertension (*n*,%)	6 (16.4)	5 (4)	0.076

Fasting glucose level (mean ± SD)	5.98 ± 1.22	3.18 ± 1.26	<0.001‡
Insulin level (mean ± SD)	14.43 ± 2.15	11.73 ± 1.17	<0.001‡
Insulin resistance (n,%)	23 (54)	0 (0)	<0.001‡
Cholesterol level (mean ± SD)	195.56 ± 18.5	172.56 ± 35.02	<0.001‡
Triglycerides level (mean ± SD)	102.07 ± 9.44	82.53 ± 7.27	<0.001‡
HDL‖ level (mean ± SD)	33.54 ± 3.57	43.7 ± 3.87	<0.001‡
Leptin level (mean ± SD)	423.08 ± 44.74	284.36 ± 56.24	<0.001‡
Metabolic syndrome (n,%)	25 (65)	3 (5)	<0.001‡
Family history (n,%)	10/40 (25)		

Table No. 2. Skin tag predictors using multivariate logistic regression

	OR*	**95% CI for B**		**P value**
		Lower	**Upper**	
Fasting glucose	3.502	0.954	12.873	0.059
Triglycerides	1.204	1.043	1.392	0.012†
HDL‡	0.553	0.385	0.800	0.003†
WC§				0.687
HTN‖				0.574

Table 3: The number of skin tags is predicted by multivariate linear regression

	Coefficient	**95% CI for B**		**P value**
		Lower	**Upper**	
WC*	0.087	-0.235	0.386	0.624
HTN†	0.145	-7.922	17.553	0.447
Fasting glucose	0.065	-2.944	4.373	0.692
Triglycerides	0.077	-0.375	0.583	0.664
HDL‡	-0.002	-1.336	1.318	0.985

Table 4: Plasma leptin level predictors using multivariate linear regression

	Coefficient	**95% CI for B**		**P value**
		Lower	**Upper**	
WC*	0.174	-0.053	1.77	0.063
HTN†	-0.052	-62.5	33.0	0.554
Fasting glucose	0.014	-10.4	11.7	0.902
Triglycerides	0.286	0.411	3.55	0.015‡
HDL§	-0.403	-8.5	-2.07	0.003‡

DISCUSSION

According to this study, STs and/or hyperleptinemia are associated with dyslipidaemia. MS was significantly associated with our patients (65%) in the univariate analysis, however, our multivariate analysis revealed statistical significance only for high triglycerides and low HDL levels. High triglycerides and low HDL levels were also significant predictors of high plasma leptin levels in multivariate linear regression analysis of plasma leptin levels.

Based on our knowledge, this is the first study to examine whether STs and leptin levels are related to MS. A study of four ST cases found that elevated lipid levels, type 2 diabetes, and cardiovascular disease are risk factors for STs [20]. A study conducted on ST cases also suggested skin tags were cutaneous findings associated with MS and heart disease risk factors, similar to our findings. The study recommends carefully evaluating these patients for heart disease and MS [21]. It is common for people to have skin tags, which last until menopause/andropause [22]. In the study, triglycerides and HDL should be measured in patients with ST and hyperleptinemia (if positive, other components of metabolic syndrome should be measured as well). In order to reduce the risk of STs and/or hyperleptinemia, we recommend that patients with STs and/or hyperleptinemia change their life style. They should stop active smoking, eliminate passive smoking, do regular exercises, reduce their weight, and change their carbohydrate diet to high protein diets. We recommend the use of polyunsaturated fatty acids, especially olive oil, omega 3, 6, and 9, for

patients with STs or hyperleptinemia who are at risk for coronary artery disease [23].

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