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Research Article

Metabolic Associations with Skin Tags

Abstract

Background: Skin tags are small, soft, pedunculated, often pigmented lesions, usually occurring on the eyelids, neck and axillae. There have been a few reports in the literature that the presence of skin tag is associated with different components of the metabolic syndrome.

Objective: To evaluate the relationship between components of metabolic syndrome (atherogenic lipid, glucose level, hypertension, and waist circumference) and other metabolic associations with skin tags.

Patients and Methods: A total of 51 patients with skin tags aged 16 to 64 years, 13 males (31.37%), 38 females (68.63%) with a mean age of (38.6 ± 12.1 SD); and 50 healthy controls aged 19 to 60 years, 13 males (30%) and 37 females (70%) with a mean age of (37.9 ± 9.4 SD) were examined in dermatology outpatient clinic of Kufa Medical School Teaching Hospital, Najaf, Iraq. Body Mass Index (BMI),waist circumference (WC),blood pressure (BP), fasting blood sugar (FBS), serum lipids including triglyceride, total cholesterol, high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), liver enzymes (AST, ALT), alkaline phosphatase and serum uric acid were measured for both study groups. The study was approved by Ethics Committee of Kufa Medical School in Iraq.

Results: There was no significant statistical difference in fasting blood sugar, serum uric acid, liver function tests, triglyceride, high density lipoprotein and very low density lipoprotein between the study groups. Patients group has showed significantly higher levels of total cholesterol and LDL, when compared with the healthy controls group ($P < 0.01$). Also patients group showed significantly higher values of BMI, blood pressure (BP), and Waist circumference (WC) compared with the healthy controls group (p = 0.0001), (p = 0.001) and ($P < 0.01$) respectively. It has been found that 37 (72.5%) of the patients and 13 (26%) of the controls meet at least three of the criteria of metabolic syndrome.

Conclusion: Total cholesterol and LDL serum levels should be checked in patients with skin tags. On the other hand, glucose, serum levels may not be as important as what is being considered in recent time.

Introduction

Part 1 / skin tags

Synonyms: Soft warts, achrochordon[1], cutaneous tag, papilloma colli, fibroma pendulum, cutaneous papilloma, fibroma molluscum, templeton skin tags [2], fibroepithelial polyps, pedunculated soft fibromas, filiform soft fibromas [3].

Definition: Skin tags are common benign connective tissue tumors of the dermis [4], composed of loose fibrous tissue [1], and presents as a soft skin colored to slightly hyperpigmented pedunculated papule [5]. These flesh-colored tumors are often raised from the surface of the skin on a fleshy stalk called a peduncle, and feel like small bags. Skin tags may be single or multiple and are typically the size of a grain of rice [2,6], but they may range in size from 1-2 mm papules on the eyelids to 1-2 cm baggy polyps on the trunk [5]. The surface of a skin tag may be smooth or irregular in appearance [6].

Three types of skin tags have been described:

- Small, furrowed papules of approximately 1-2 mm in width and height, located mostly on the neck and the axillae.

- Single or multiple filiform lesions of approximately 2 mm in width and 5 mm in length occurring elsewhere on the body.

- Large, pedunculated tumor or nevoid, baglike, soft fibromas that occur on the lower part of the trunk [7].

The most common site of skin tag is on the sides of the neck, where they may be mixed with typical small, sessile, seborrheic keratoses [1]. They are also seen frequently in the axillae, eyelids, and less often on the trunk and groins, where the soft pedunculated growths often hang on thin stalks [2], perianal skin are also frequently involved [2,8] and this has now been named infantile perianal pyramidal protrusions. This occurs in young children usually girls, in the midline anterior to the anus. This reduces with time and no treatment is necessary [2].

Skin tag may occur at unusual sites of the body. A huge skin tags have been described on the penis [9]. A lymphedematous skin tag of the glans penis unassociated with condom catheter use also has been described [6]. Skin tags of the oral mucosa, anus, and vulvovaginal areas may be found [7].

Skin tags are usually asymptomatic, but on occasion can become painful secondary to irritation or torsion and infarction [5]. Patients may complain of pruritus or discomfort when an acrochordon is

snagged by jewelry or clothing [7]. Vulvovaginal skin tag may be associated with itching without the symptom being the result of fungal infection [10]. Skin tags are harmless, and may not grow or change over time [6].

Incidence: The condition is very common, particularly in middle-aged and elderly people [9-12] and their incidence increases with age, and close to 46% - 50% of all individuals have at least one skin tag [5,7], with nearly 60% of individuals acquiring them by the age of 69 years [2]. An equal prevalence of skin tags exists in males and females [7], but some studies suggested that skin tags are common particularly in middle age and elderly women [9-12], where they found together with seborrheic keratosis [1].

Causes and precipitating factors: Frequent irritation in areas of skin friction [11], seems to be an important causative factor, especially in persons who are obese [4,13,14]. An opinion also exists that skin tags are simply the effect of skin aging, with many factors responsible for their development [15]. Hormone imbalances may facilitate the development of skin tags (ex. high levels of estrogen and progesterone during pregnancy, high levels of growth hormone in acromegaly). Epidermal growth factor and alpha tissue growth factor have also been implicated in the development of tumors such as these [15].

Whether any infective factors initiate acrochordon growth is still not clear. Human papillomavirus types 6 and 11 DNA was found in a high percentage of skin tag biopsy samples obtained from 49 white patients. According to the authors of the study, viral infection should be considered as a pathogenic cofactor [15].

Skin tags associated with fibrofolliculomas and trichodiscomas have been described as components of Birt-Hugg-Dube syndrome, an autosomal dominant disorder. They have been reported to accompany other neoplasms, especially tumors of the gastrointestinal tract and kidneys. Neoplasms are suggested to produce and release growth factors that cause skin tags growth in to the circulation [7], whereas in Cowden disease the skin tags are sclerotic fibroma [5].

An association with type - 2 diabetes mellitus has been observed [16-19]. A study of 118 research subjects with acrochordon reported an incidence of 40.6% of either overt type - 2 diabetes mellitus or impaired glucose tolerance. Reports exist suggesting that the mechanism is through the effect of insulin and glucose starvation [20-22]. The previous study showed no correlation between the location, size, color, or number of skin tags with impairment of glucose tolerance [7]. They often increase in number when the patient is gaining weight or during pregnancy, and may be related to the growth hormone-like activity of insulin.

In patients preselected for gastrointestinal complaints, skin tags appear to be more prevalent in those with colonic polyps. This association has not been proved for the general population [2,7].

A family history of acrochordon sometimes exists [7]. Observations of skin tags and obese people were the first to indicate a genetic correlation to skin tags. Scientists were looking for the reasons why some patients had skin tags and other patients didn't and noted that skin tags were seen to consistently exist within families. A logical

conclusion was that there was a link in the DNA of affected people [6].

The skin tags may represent a cutaneous sign for impaired carbohydrate or lipid metabolism [9], liver enzyme abnormalities and hypertension [15]. In one study report that skin tags are associated with various components of the metabolic syndrome [9], no data in the literature show that the presence of skin tags is associated with serum high-sensitive C- reactive protein, uric acid, free fatty acid and leptin level [23].

Mast cells and tumor necrosis factor "TNF"-α may play a role in the pathogenesis of skin tags following trauma to the skin, in the form of friction, "TNF-related apoptosis-inducing ligand" is upregulated and can induce mast cell migration into the skin through the release of chemokines. Mast cells in turn release TNF-α. The latter, through direct or indirect interactions with fibroblasts and keratinocytes could initiate some of the changes that lead to the formation of skin tags [24].

Part 2 / metabolic syndrom

Metabolic syndrome (syndrome X, insulin resistance syndrome) refers to a cluster of known disorders that increase the risk for morbidity and mortality from cardiovascular disease and type - 2 diabetes. Risk for type - 2 diabetes mellitus increases five to nine fold with metabolic syndrome [14].

Metabolic syndrome (Table 1) is a complex cluster of several risk factors within a single patient according to the National Cholesterol Education Program / Adult Treatment Panel (ATP) lll, which are directly related to the incidence of coronary heart disease [20,23].

Evolving perspectives on the definition of metabolic syndrome

In addition to the ATP III clinical identification of the metabolic syndrome (Table 1) various organizations have set forth clinical criteria for its diagnosis [25]. Although similar in many aspects to other guidelines, the World Health Organization clinical criteria for the metabolic syndrome regard insulin resistance as a required component for diagnosis of the syndrome [25-27]. Furthermore any two of five other risk factors are regarded as sufficient to meet the definition of metabolic syndrome. Requiring objective evidence of insulin resistance may provide a stronger prediction of type - 2 diabetes mellitus than ATP lll; however, consistent with ATP lll findings, type - 2 diabetes mellitus does not exclude a diagnosis of the metabolic syndrome [25].

The American Diabetes Association recently conducted an

Table 1: National Cholesterol Education Program (NCEP), Adult Treatment Panel III (ATP lll). Diagnosis of metabolic syndrome includes at least 3 of the following: [24].

- Large waist circumference < 102 cm (40 inches) for men, and < 88 cm (35 inches) for women.
- Serum triglyceride (TG) levels ≥ than 150 mg/dl.
- Level of high-density lipoprotein cholesterol (HDL-C) > 40 mg/dl for men, and > 50 mg/dl for women.
- Hypertension: Blood Pressure (BP) ≥ than 130/85 mmHg.
- Fasting glucose level (FBS) ≥ than 110 mg/dl.

extensive review of the literature relating to the metabolic syndrome and uses the term metabolic syndrome to refer to a clustering of specific cardiovascular disease risk factors whose underlying pathophysiology is thought to be related to insulin resistance [27]. The American Diabetes Association acknowledges that certain cardiovascular disease risk factors are prone to cluster. However, their recommendation is that further research is needed (including studies that investigate the pathogenesis of the metabolic syndrome) and that clinicians should evaluate and treat all cardiovascular disease risk factors without regard to whether a patient meets the criteria for diagnosis of the metabolic syndrome [27].

World health organization criteria for metabolic syndrome: [28,29]

Insulin resistance, identified by one of the following:

- Type - 2 diabetes mellitus

- Impaired fasting glucose

- Impaired glucose tolerance

- Or for those with normal fasting glucose levels (> 110 mg/dL), glucose uptake below the lowest quartile for background population under investigation under hyper-insulinemic or eu-glycemic conditions.

Plus any two of the following:

- Antihypertensive medication and / or high blood pressure (≥ than 140 mm Hg systolic, or ≥ than 90 mm Hg diastolic).

- Plasma triglycerides ≥ than 150 mg/dL (1.7 mmol/L).

- High-density lipoprotein cholesterol > 35 mg/d (0.9 mmol/L) in men, or > 39 mg/dL (1.0 mmol/L) in women.

- Body mass index of < 30 kg/m2 and/or waist to hip ratio of < 0.9 in men, or less than 0.85 in women.

- Urinary albumin excretion rate ≥ than 20 ~ tg/min or albumin to creatinine ratio ≥ than 30 mg/g.

Atherogenic dyslipidemia clinically presents as elevated serum triglyceride levels, increased small dense low-density lipoprotein particles, and decreased levels of high density lipoprotein - cholesterol [29,30]. All of these abnormalities have been implicated as being independently atherogenic. The three abnormalities of elevated serum triglycerides, increased small dense low-density lipoprotein particles, and low high density lipoprotein - cholesterol have been termed the atherogenic lipoprotein phenotype [31] or, more simply, the lipid triad. This multiplex array of lipid abnormalities is a powerful risk factor for coronary heart disease, defined as angina pectoris, unstable angina, myocardial infarction, or coronary death [32,33].

Etiology: Risk factors for metabolic syndrome include family history, poor diet, and inadequate exercise.

Metabolic syndrome is thought to be caused by adipose tissue dysfunction and insulin resistance. Dysfunctional adipose tissue also plays an important role in the pathogenesis of obesity-related insulin resistance [34]. Both adipose cell enlargement and infiltration of macro-phages in to adipose tissue result in the release of pro inflammatory cytokines and promote insulin resistance [35]. Insulin resistance appears to be the primary mediator of metabolic syndrome [36]. Insulin promotes glucose uptake in muscle, fat, and liver cells and can influence lipolysis and the production of glucose by hepatocytes [37]. Additional contributors to insulin resistance include abnormalities in insulin secretion and insulin receptor signaling, impaired glucose disposal, and pro inflammatory cytokines. These abnormalities, in turn, may result from obesity with related increases in free fatty acid levels and changes in insulin distribution (insulin accumulates in fat). The distribution of adipose tissue appears to affect its role in metabolic syndrome. Fat that is visceral or intra-abdominal correlates with inflammation, whereas subcutaneous fat does not. Abdominal fat is known to produce potentially harmful levels of cytokines, such as tumor necrosis factor, adiponectin, leptin, resistin, and plasminogen activator inhibitor. Lifestyle factors such as alcohol consumption, cigarette smoking, and physical activity have been reported to affect an individual's metabolic profile [37,38]. Studies have also reported an inverse relationship between physical activity and certain components of metabolic syndrome such as waist circumference, high density lipoprotein - cholesterol and blood pressure [38].

Clinical Presentation of metabolic syndrome: may include the following:

- Hypertension.

- Hyperglycemia.

- Hypertriglyceridemia.

- Reduced high-density lipoprotein cholesterol.

- Abdominal obesity.

- Chest pains or shortness of breath: Suggesting the rise of cardiovascular and other complications.

- Acanthosis nigricans, hirsutism, peripheral neuropathy, and retinopathy: In patients with insulin resistance and hyperglycemia or with diabetes mellitus.

- Xanthomas or xanthelasmas: In patients with severe dyslipidemia [39].

Diagnosis: According to guidelines from the National Heart, Lung, and Blood Institute and the American Heart Association, metabolic syndrome is diagnosed when a patient has at least 3 of the following five conditions:

- Fasting glucose ≥110 mg/dL (or receiving drug therapy for hyperglycemia).

- Blood pressure ≥130/85 mm Hg (or receiving drug therapy for hypertension).

- Triglycerides ≥150 mg/dL (or receiving drug therapy for hypertriglyceridemia).

- High density lipoprotein – cholesterol <40 mg/dL in men or < 50 mg/dL in women (or receiving drug therapy for reduced high density lipoprotein – cholesterol).

Waist circumference ≥102 cm (40 in) in men or ≥88 cm (35 in) in women; if Asian American, ≥90 cm (35 in) in men or ≥80 cm (32 in) in women [40].

Part 3 / association between skin tags and metabolic syndrom

Multiple skin tags have been associated with abnormalities in the glucose metabolism, specifically type - 2 diabetes, hyperinsulinemia and insulin resistance. Insulin resistance is a state in which a given concentration of insulin produces a less than expected biological effect. Obesity is the most common cause. This is followed by compensatory hyperinsulinemia to maintain normal glucose and lipid homeostasis [40,41].

Different methods are available for assessment of insulin resistance, of which calculation of the homeostasis model assessment of insulin resistance provides a useful approach [41,42]. Hypertension, diabetes and metabolic syndrome were significantly more frequent in patients with acrochordons than the control group, according to the study on a total of 192 patients with at least one skin tag and 104 controls having no skin tag seen at an academic outpatient dermatology clinic were involved. According to regression analysis, the number of acrochordons increased in patients with higher body mass index values, 2-h plasma glucose, triglyceride and low density lipoprotein - cholesterol levels and lower high density lipoprotein - cholesterol levels. These results support the suggestion that acrochordons are associated with the components of metabolic syndrome [42,43] and the risk of atherosclerosis and cardiovascular disease [44]. One study shows that the skin tags are not associated with increased incidence of obesity compared to the general population. On the other hand, skin tags are associated with impaired carbohydrate metabolism, and may serve as means for identifying patients at increasing risk of having diabetes mellitus [19], yet the relation of skin tags to obesity is still a matter of controversy [45].

Clinical and metabolic glucose/insulin characteristics of men with multiple (8 or more) skin tags on the neck were compared with a control group with few or none. One-third of the study group had acanthosis nigricans. Multiple skin tags were more sensitive than acanthosis nigricans in identifying those with alterations in the glucose/insulin metabolism, although less specific. Multiple skin tags should raise suspicion of insulin resistance or hyperinsulinemia [46].

The possible association of skin tag with diabetes mellitus was first mentioned in 1951. Since then, a few clinical studies have been conducted to examine this hypothesis with conflicting results. Diabetes or impaired glucose tolerance had greater number of skin tags compared to normo-glycemic ones, but there was no significant difference between number of skin tags in diabetes and impaired glucose tolerance group, in addition, patients with more than 30 skin tags (designated as high number) had significantly higher incidence of impaired carbohydrate metabolism than patients who had less than 30 skin tags.

There is no positive correlation between number of skin tags and body mass index, similarly, the mean number of skin tags in obese, over weight and normal weight was not significantly different. No correlation was found between the anatomical location of skin tag and the presence of abnormal carbohydrate metabolism, except for skin tags under the breast in women [47]. Specific dermatoses as skin tags, striae distensae and plantar hyperkeratosis, could be considered as a cutaneous stigma of severe obesity. Although the physiological mechanisms are still unknown, finding has not been previously described and that this may constitute new field in the research on obesity [48]. Acrochordons were found to be closely associated with pseudo-acanthosis nigricans, seborrheic keratosis, obesity and non-insulin dependent diabetes mellitus [4]. A study included Thirty-six patients with skin tags and 22 healthy controls, the mean levels of body mass index, homeostasis model assessment of insulin resistance, and total cholesterol were significantly higher in patients than in controls.

So skin tags may not be innocent tumoral proliferations; instead, follow-up of such patients with regard to the development of diseases associated with atherosclerosis may beneficial [49].

Aim of the study

To evaluate the possible relationship between components of metabolic syndrome (atherogenic lipid, serum glucose level, hypertention and waist circumference); and other metabolic associations with the occurrence of skin tags .

Patients and Methods

A total of 51 patients and 50 healthy controls, matched in age and sex, were included in the study. Patients and controls were recruited from Dermatology Outpatient Clinic of Kufa Medical School Teaching Hospital, Najaf, Iraq. All subjects were examined by a dermatologist; patients were defined as persons with skin tags at any body site and controls as persons having no skin tag. Skin tag was diagnosed clinically as a fleshy pedunculated soft protrusion skin colored or brownish, affecting the flexural areas or face. Personal history of hypertention, diabetes, hyperlipidemia, drug intake, smoking, missed period in female, and family history of skin tags was recorded for both groups.

Exclusion criteria from the study for both groups were:

- Patients receiving drugs with a known antihyperlipidemic effect.

- Pregnant women.

- Patients who are known cases of hypertension or receiving drugs with a known antihypertensive effect.

- Patients who are known cases of diabetes mellitus or receiving drugs with a known hypoglycemic effect.

The height, weight, waist circumference (in inch) and body mass index (BMI) of patients and controls were measured.

Body mass index "BMI" was calculated by dividing body weight to height square (kg/m2). Patients were considered according to their BMI:

- BMI ≤ 18 as thin.

- BMI between 19 and 25 as normal.

Table 2: Clinical characterestics of study groups.

Variables		Patient (mean ± SD)	Control (mean ± SD)	P value
BMI		32.5±6.2	27.1±5.3	0.0001
Blood pressure	Systolic	136.3±16.2	126.8±9.4	0.001
	Diastolic	84.1±11.8	75±6.6	0.001
Waist Circumference	Female	37.7±4.7	34.7±3.9	0.005
	Male	39.7±3.8	34.8±3.2	0.001
Smoking	Positive	5 (9.8%)	2 (4%)	0.25
	Negative	46 (90.2%)	48 (96%)	
Family history	Positive	50(98%)	4(8%)	0.0001
	negative	1(2%)	46 (92%)	

Table 3: Liver function tests, fasting blood sugar and serum uric acid values in study groups.

	Patients (mean ± SD)	Controls(mean±SD)	P value
AST	17.2±6.3	18.9± 8.4	0.263
ALT	21.2±9.4	20.9± 7.9	0.943
ALP	107.8±27.9	107.4±34.9	0.958
FBS	112.9±38.7	106.1±23.6	0.23
SUA	4.7±1.2	4.5±.83	0.28

Table 4: Lipid profile in study groups.

	Patient (mean±SD)	Control(mean±SD)	P value
Cholesterol	**204.5±43.7**	**177.02±35.8**	**0.001**
TG	151.8±69.8	134.3± 59.9	0.215
HDL	34.3±11.5	37.04±8.7	0.178
VLDL	29.9± 10.7	27± 12.3	0.264
LDL	137.1±37.8	113.1±31.4	0.001

Table 5: Occurance of metabolic syndrome in study groups.

		Group		Total No. (%)	P value
		Patient No. (%)	Control No. (%)		
Metabolic syndrome	Present	37(72.5%)	13(26%)	50(49.5%)	0.0001
	Absent	14(27.5%)	37(74%)	51(50.5%)	
Total		51(100%)	50(100%)	101(100%)	
*Odd ratio=7.5.					

- BMI between 26 and 29 as overweight.

- BMI ≥30 as obese.

Where the height of patients was measured by using a rubbery tape measure and approximated to nearest 0.5 cm and weight of patients was taken by weight measuring device. Waist circumference was measured (in inch) by a rubbery tape measure, by finding the top of hip bone and the bottom of the last rib, then ask the person to breathe out normally and place the tape measure midway between these points and wrap it around the waist. Blood preasure was measured to both groups by sphygmomanometer.

All patients and controls were informed about the aim and procedure of the study. Investigations were performed for both groups in the study including liver function tests (Alanine transaminase "ALT", Aspartate transaminase "AST", Alkaline phosphatase "ALP") and serum uric acid (by autoanalyzer device). Blood samples of the patients and controls were taken after (at least) an eight-hour starvation, to measure fasting blood sugar, serum total cholesterol,

triglyceride, and High density lipoprotein – cholesterol values (by autoanalyzer device).

Low density lipoproten – chelesterol and very low density lipoproten – chelesterol values were calculated according to the following formulas:

- Very low density lipoproten – chelesterol = triglyceride / (divided by) 5.

- Low density lipoproten – chelesterol = cholesterol – (minus) (Very low density lipoproten – chelesterol + High density lipoprotein – cholesterol).

Normal values (according to the standards of the Teaching Hospital Laboratory) were as follows:

- Total cholesterol : 0-199 mg/dl.

- Triglyceride : 0-149 mg/dl.

- High density lipoproten : 40-60 mg/dl.

- Low density lipoproten : 100-129 mg/dl.

- Very low density lipoproten : 5-40 mg/dl.

- Uric acid : 3.50-7 mg/dl.

- Alanine transaminase "ALT": 0-55U/L.

- Aspartate transaminase "AST": 5-34U/L.

- Alkaline phosphatase "ALP": 40-150U/L.

- Fasting blood sugar: 70-99 mg/dl.

According to Adult Treatment Panel III criteria of metabolic syndrome (Table 1), those who met at least three criteria were included in a group called (metabolic syndrome group).

Statistical analysis

All the results were expressed as means ± (Standard Deviation "SD") values. The significance of the difference between the groups was assessed by unpaired Student's t-test for continuous variables. The chi-square test or Fischer's Exact test was used for testing prevalence between groups, Pie charts and Bar chart were used as needed. The statistical analysis was performed using Statistical Package for the Social Science "SPSS" Version 20 program, and P values of < 0.05 were considered as significant.

Ethical approval

This study has been approved by the Ethics Committee of Kufa Medical School, Iraq. All individuals in study groups have informed signed consents.

Results

A total of 51 patients with skin tags with ages of 16 to 64 years, including 13 males (31.37%) and 38 females (68.63%) with a mean age of (38.6 ± 12.1 SD), (Figures 1,2); in addition to 50 healthy controls aged 19 to 60 years, 13 males (30%) and 37 females (70%), (Figure 3) with a mean age of (37.9 ± 9.4 SD); were examined in the present study. A positive family history of skin tags was present in 50 (98%)
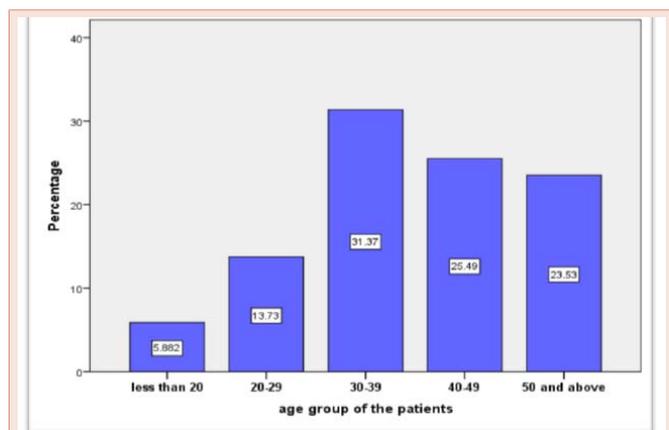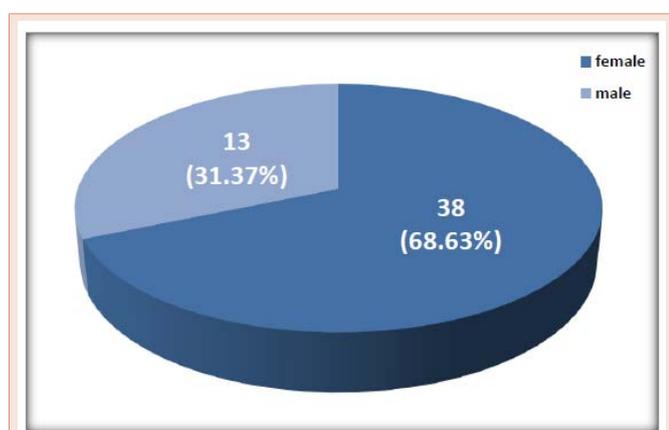
Figure 1: Age distribution in patients group.

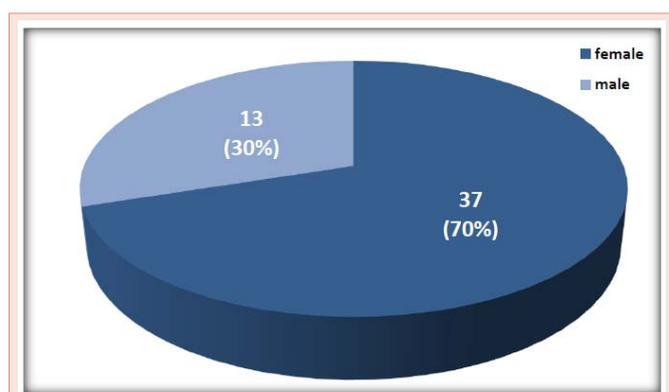

Figure 2: Sex distribution in patients group.

Figure 3: Sex distribution in controls.

of patients and 4 (8%) of controls. On the other hand, 5 (9.8%) of patients and 2 (4%) of controls were smokers (Table 2). There was no significant difference in fasting blood sugar, serum uric acid or liver function tests between the two groups (Table 3).

Patients group showed significantly higher levels of total cholesterol and low density lipoproten, when compared with the healthy controls group (P = 0.001), while no significant differences in triglyceride, high density lipoprotein and very low density lipoprotein were present between the two groups (Table 4) . Also patients group showed significantly higher values of body mass index, blood pressure and waist circumferenceV when compared with the healthy controls (p = 0.0001), (p = 0.001) and (P < 0.01) respectively; (Figures 4,5 and Table 2).

Depending on the Adult Treatment Panel III criteria for diagnosis of metabolic syndrome that was mentioned (Table 1), it was found that 37 (72.5%) of patients and 13 (26%) of controls met at least three of the criteria of metabolic syndrome; while 14 (27.5%) of the patients and 37 (74%) of controls failed to meet those criteria, with a p value of (P = 0.0001) which was highly significant (Table 5).

Discussion

In the present study we found that (80.4%) of the patients were above the age of 30 years, with the larger percentage occur between (30 to 39) years of age, while (19.6%) of the patients were below the age of 30 years, and they were mostly female (68.63%), and this support the suggestion that skin tags are more common in women or may be explained by the fact that women are seeking medical interference for cosmetic purposes more than men .

Family history was positive in (98%) of the patients and in only (8%) of controls; and this supports the role of genetic factor in the pathogenesis of skin tags.

Multiple skin tags are frequently associated with non-insulin-dependent diabetes mellitus and obesity [19]. Obesity is a factor that has been associated with the development of skin tags [43]. In the present study, body mass index of patients was significantly higher than controls with a (P=0.0001); and patients were mostly obese (68.63%), while (19.61%) were over weight and these results support the suggestion of association of skin tags with obesity. According to the study of Shaheen M.A. et al., which agrees with older studies, a suggestion was made that android pattern of obesity is to be more predictive of insulin resistance than body mass index, and accordingly, waist circumference appears to be the most related criteria of the metabolic syndrome that correlates positively with the number of skin tags in different body mass index patients [46]. In the present study we found the waist circumference which is one of the components of metabolic syndrome is significantly higher in the patients group when compared with controls (P = 0.005 for females, and P = 0.001 for males) . So we could conclud that skin tags show a statistically significant relationship with obesity.

A supposed relation is found between diabetes millettus and skin tags. A study done by Rasi et al. [8], investigated oral glucose tolerance test with 75g glucose and showed an increased risk of diabetes mellitus in patients with skin tags . However, we could not find this kind of relationship in the present study where we found no significant statistical difference in fasting serum glucose levels between the groups ; and this might be due to the fact that we have not tested our patients for oral glucose tolerance test. On the other hand, our result is similer to that obtained from a study done by Gorpelioglu C et al.
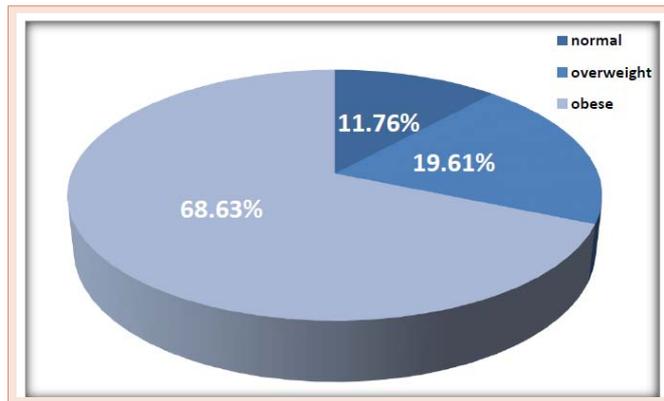
Figure 4: BMI distribution in patients group.
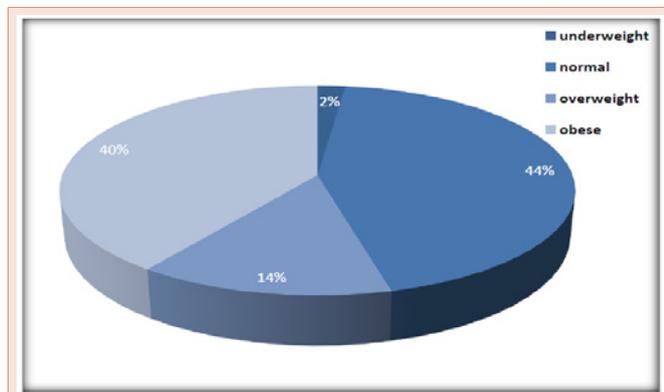
Figure 5: BMI distribution in controls.

[9], but in their study the patients and controls had a similar body mass index (28.7 ± 7.9) ; therefore, they thought that the relationship between skin tags and diabetes mellitus might be associated with the patients having obesity and obesity related glucose intolerance, while in the present study the body mass index is significantly higher in the patients when compared with controls group (p > 0.0001). Similarly, in another study, Marthur et al., estimated insulin resistance in 10 patients with multiple skin tags and 10 control subjects matched for age, sex and body weight. They concluded that skin tags are not markers of insulin resistance and it is possible that epidermal growth factor or other growth factors may play a role in the pathogenesis of skin tags [21].

There are only few studies about the relationship between skin tags and atherogenic lipid profile. Crook investigated serum lipid profile in four patients with skin tags and found increased serum triglyceride and decreased HDL cholesterol [50]. Erdogan et al., found increased total cholesterol in 36 patients with skin tags, when compared with 22 healthy controls [51]. Gorpelioglu C et al. [9], found total cholesterol levels and low density lipoproten serum levels were higher in patients with skin tags, when compared with the healthy control group. The last two studies meet the results of the present study, that showed the total serum cholesterol and low density lipoproten serum levels were significantly higher in patients with skin tags in comparison

to healthy controls (P = 0.001) for both, however, there was no statistically significant difference in the serum triglycerides, high density lipoproten, very low density lipoproten serum levels in both groups (P= 0.215, P=0.178, P= 0.264) respectively.

Skin tags could represent a cutaneous sign for impaired carbohydrate or lipid metabolism, liver enzyme abnormalities and hypertension [52,53].

Insulin resistance syndrome or metabolic syndrome is a collection of health risks that increases the chance of developing heart disease, stroke and diabetes. Various risk factors have been included and the factors generally accepted as being characteristic of this syndrome include abdominal obesity, raised blood pressure, atherogenic dyslipidaemia and insulin resistance with or without glucose intolerance [54]. Hypertension, diabetes and metabolic syndrom were significantly more frequent in patients with skin tags than the control group, according to the study on a total of 192 patients with at least one skin tag and 104 controls having no skin tag seen at an academic outpatient dermatology clinic were involved . The acrochordon group showed significantly higher values of body mass index, higher levels of aspartate amino transferase, alanine amino transferase, gamma-glutamyl transferase, alkaline phosphatase, triglycerides, triglycerides and low density lipoproten – cholesterol and significantly lower levels of high density lipoproten – cholesterol when compared with the control group. The number of skin tags is increased in patients with higher body mass index values, 2-h plasma glucose, triglycerides and low density lipoproten – cholesterol levels and lower high density lipoproten – cholesterol levels.

These results support the suggestion that skin tags are associated with the components of metabolic syndrome, and with the risks of atherosclerosis and cardiovascular disease [55].

In the present study the summery of results that explain the associations between skin tags and components of metabolic syndrome includes: Waist circumference and blood pressure were significantly higher in patients with comparison to controls group. While the triglycerides, high density lipoproten, fasting blood sugar, showed no statistically differences between the two groups. But generally, we found 37 (72.5%) of the patients and 13 (26%) of controls meet at least three of the criteria of metabolic syndrome. These results are also in agreement with a study proposed that skin tags are cutaneous findings frequently associated with the risk factors for metabolic syndrom and heart disease, and recommended that these patients should be carefully evaluated for metabolic syndrom and heart disease (24). Our results showed no association between skin tags and liver enzymes abnormalities or serum uric acid, and there were no significant differences between the values of liver enzymes (Aspartate transaminase "AST", Alanine transaminase "ALT" and Alkaline phosphatase "ALP") between the patient and control groups (p=0.263, p=0.943, p=0.958) respectively.

Conclusions and Recommandations

We may propose that skin tags may be one of the important skin markers of metabolic disorders and may attract physicians and dermatologist for further investigation as it is proved to be not just a cosmetic problem .

The results of this study advice the screening of patients with skin tags for hypercholesterolemia, increased level of low density lipoproten (when positive, other components of metabolic syndrome are preferably to be measured).

This leads us to recommend the change of life style of patients with skin tags and / or hyperlipidemia, as stopping active smoking and prevention of passive smoking, regular exercises, weight reduction, changing carbohydrate diets into high protein diets.

Knowing that diets rich in polyunsaturated fatty acids as olive oil, omega 3, 6 and 9 fatty acids supplementation can decrease the risk of coronary atherosclerosis, we recommend their use for patients with skin tags and/or hyperlipidemia.

Because our study consisted of a limited number of patients and controls from asingle population, further studies done with larger patient groups will be beneficial in elucidating the relationship between skin tags and atherosclerotic risk factors.

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