

# A clinicoepidemiological study of skin tags and their association with metabolic syndrome

## Współwystępowanie włókniaków miękkich z zespołem metabolicznym – aspekty kliniczno-epidemiologiczne

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### KEY WORDS:

skin tags, metabolic syndrome, acanthosis nigricans, insulin resistance.

### SŁOWA KLUCZOWE:

włókniaki miękkie, zespół metaboliczny, rogowacenie ciemne, insulinooporność.

### ABSTRACT

**Introduction.** Skin tags are known to be associated with several systemic diseases such as diabetes mellitus, obesity, dyslipidemia and cardiovascular diseases. Only a few Indian studies have investigated patients with skin tags for underlying metabolic complications.

**Objective.** To assess the clinico-epidemiological profile of patients with skin tags and evaluate them for underlying metabolic abnormalities.

**Material and methods.** All the patients reporting skin tag(s) at the dermatology outpatient department from October 2013 to September 2014 were included in the study. A detailed general, cutaneous and systemic examination was carried out. The data were analyzed using the  $\chi^2$  test. A *p*-value < 0.05 was considered significant.

**Results.** Out of 165 enrolled patients, 112 (67.88%) completed the study protocol. Females outnumbered males, the M : F ratio being 1 : 1.11. Most patients (32; 28.57%) were in the age group of 31–40 years. The majority of the patients (77; 68.75%) reported after 1 year of noticing the lesions. The most commonly affected site was the neck (99; 88.39%) followed by the axilla (53; 47.32%). Acanthosis nigricans was the most common skin disease associated with skin tags (37; 33.03%). The diagnostic criteria for metabolic syndrome were fulfilled by 47 (41.96%) patients. The majority of the patients (70; 62.5%) were either overweight or obese. Abnormal glucose tolerance and hypertension were found in 41 (36.6%) and 37 (33.03%) of the patients respectively. Above optimal LDL cholesterol was the most common lipid abnormality, detected in 64 (56.25%) of the cases. Patients with 11 or more skin tags lesions and those with involvement of the thigh, axilla or neck were more likely to have metabolic syndrome.

**Conclusions.** Patients with skin tags should be screened for concomitant diseases such as diabetes, hypertension, dyslipidemia and cardiovascular disease. Early detection of these complications followed by appropriate lifestyle changes and/or drug therapy would be beneficial in terms of reducing the considerable morbidity and mortality.

### STRESZCZENIE

**Wprowadzenie.** Włókniaki miękkie (nitkowate, ang. *skin tags*) występują u pacjentów z cukrzycą, otyłością, dyslipidemią i chorobami układu krążenia. Tylko w kilku pracach indyjskich poszukiwano współistniejących z włókniakami miękkimi chorób metabolicznych.

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**Cel pracy.** Analiza kliniczno-epidemiologiczna pacjentów z włókniakami miękkimi oraz ocena współistniejących zaburzeń metabolicznych.

**Materiał i metodyka.** Do badania włączono wszystkich pacjentów z włókniakami miękkimi, którzy zgłosili się do ośrodka autorów w okresie od października 2013 do września 2014 roku. Przeprowadzono dokładne badanie podmiotowe i przedmiotowe z oceną dermatologiczną. Uzyskane dane poddano analizie statystycznej, używając testu  $\chi^2$ . Wyniki uznano za istotne statystycznie dla wartości  $p < 0,05$ .

**Wyniki.** Badanie ukończyło 112 (67,88%) ze 165 zakwalifikowanych pacjentów. Stosunek kobiet do mężczyzn wynosił 1,11 : 1. Większość pacjentów (32; 28,57%) była w grupie wiekowej 31–40 lat i zgłosiła się do lekarza po roku od zauważenia zmian skórnych (77; 68,75%). Włókniaki występowały najczęściej na szyi (99; 88,29%) i w dołach pachowych (53; 47,32%). Rogowacenie ciemne było najczęstszą chorobą towarzyszącą (37; 33,03%) włókniakom miękkim. Kryteria diagnostyczne zespołu metabolicznego spełniało 47 (41,9%) badanych; u większości pacjentów (70; 62,5%) obserwowano otyłość lub nadwagę. Nietolerancję glukozy oraz nadciśnienie tętnicze stwierdzono odpowiednio u 41 (36,6%) i 37 (33,03%) badanych. Najczęstszym odchyleniem w lipidogramie było zwiększone stężenie frakcji LDL cholesterolu (64; 56,25%). Obecność 11 lub więcej włókniaków zlokalizowanych w pachwinach, pachach i na szyi była związana z występowaniem zespołu metabolicznego.

**Wnioski.** Pacjenci z włókniakami miękkimi powinni być badani w kierunku cukrzycy, nadciśnienia tętniczego, dyslipidemii i chorób układu sercowo-naczyniowego. Wczesne wykrycie tych zaburzeń, modyfikacja stylu życia i włączenie odpowiedniego leczenia farmakologicznego mogą znacznie zmniejszyć zachorowalność i śmiertelność z powodu zaburzeń metabolicznych.

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## INTRODUCTION

Skin tags (ST) are common, benign skin lesions composed of loose fibrous tissue and occurring mainly on the neck and major flexures as small, soft, pedunculated protrusions [1]. Apart from their cosmetic impact, they have now been linked to various metabolic complications [2, 3] such as diabetes mellitus (DM), dyslipidemia, obesity and cardiovascular diseases, and may therefore serve as a marker of underlying systemic disorders. The pathogenesis of ST is not fully understood; however, insulin resistance (IR) and hyperinsulinemia play an important role [4]. Other proposed pathogenetic mechanisms involve mast cells [5], leptin [2, 6], various growth factors [7], inflammatory mediators [8], estrogens [9], androgens [9] and HPV infection [10]. Metabolic syndrome (MS) [4] is defined as a constellation of metabolic abnormalities that confer increased risk of cardiovascular diseases and DM. Its major clinical features are central obesity, hypertriglyceridemia, low high-density lipoprotein cholesterol (HDL-C), hyperglycemia and hypertension (HT) [11]. Peripheral IR is believed to be the root cause of MS also [4]. Several studies [2, 3,

12, 13] have documented the association of ST with various components of MS.

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## OBJECTIVE

Our study was carried out to determine the prevalence of ST and to assess their association with various components of MS.

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## MATERIAL AND METHODS

Approval for the study was obtained from the Institutional Ethics Committee. All the patients reporting with skin tag(s) at the dermatology outpatient department from October 2013 to September 2014 were included. Informed consent was taken from all the participants.

A detailed general, cutaneous and systemic examination followed by relevant investigations was carried out. The findings were recorded in a proforma for data analysis and interpretation.

Diabetes mellitus and HT were diagnosed according to American Diabetes Association (ADA) [14] and the Seventh Report of the Joint National Com-

mittee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VII) criteria [15] respectively. Serum lipid levels were analyzed as per the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) [16]. Body mass index (BMI) was calculated as weight (in kg)/height<sup>2</sup> (in m<sup>2</sup>), and values were interpreted according to World Health Organization (WHO) [17] guidelines (Table 1).

Metabolic syndrome was diagnosed using updated NCEP ATP III criteria [18]. A diagnosis was made when three or more of the following criteria were present:

1. Waist circumference of more than 102 cm in men or more than 88 cm in women.
2. Blood pressure level of 130/85 mm Hg or higher or use of antihypertensive medication.
3. Fasting plasma glucose levels of 100 mg/dl or higher or on treatment for elevated glucose.
4. Fasting triglyceride (TG) levels of 150 mg/dl or higher or on drug treatment for elevated TG.
5. Fasting high-density lipoprotein cholesterol (HDL-C) level of less than 40 mg/dl in men or less than 50 mg/dl in women or on treatment for reduced HDL-C.

Based on the fulfillment of these criteria, the patients were divided into two groups – patients with MS and patients without MS. The two groups were compared with respect to age and sex distribution, duration, number, site, color, morphology of ST, associated symptoms and skin disorders.

### Statistical analysis

Statistical analysis was carried out using the  $\chi^2$  test.  $P < 0.05$  was considered statistically significant.

### RESULTS

Out of 165 patients with ST, 112 (67.88%) patients completed the study protocol. There was a slight female preponderance (1.11 : 1). The age group most commonly affected (32; 28.57%) was 31–40 years. The majority of patients (77; 68.75%) reported after one year from noticing the lesions. Multiple site involvement and multiple lesions were observed in 76 (67.86%) and 104 (92.86%) cases respectively. The most common ST location was the neck (99; 88.39%) followed by the axilla (53; 47.32%). The lesions were pedunculated (90; 80.36%) in most of the patients. Acanthosis nigricans (AN) was the most common associated skin disease (37; 33.03%), more frequently observed in females. Nearly one third of patients (34; 30.36%) had a family history. The demographic and clinical details are shown in Table 2.

Forty-seven (41.96%) patients fulfilled the diagnostic criteria for MS. Central obesity and low HDL-C were more common in females compared to males. Seventy patients were either overweight or obese (62.5%). Seventy-eight (69.64%) were prehypertensive or hypertensive and 41 (36.6%) were either prediabetic or diabetic. Lipid abnormalities were detected in 66 (58.92%) cases (Table 3).

Metabolic syndrome was commonly associated with itchy ST, number of lesions  $\geq 11$  and lesions on the thigh, axilla or neck. AN was the most commonly associated skin disease in both compared groups. The clinical profile of patients with and without MS is shown in Table 2.

### DISCUSSION

Skin tags are common, but their exact prevalence is difficult to determine in view of their asymptomatic nature. This was seen in our study too, where most of the patient reported after a year. We observed a slight female preponderance, consistent with other studies [3, 12, 19, 20]. Like previous studies [2, 20, 21], we observed that skin colored and pedunculated lesions tend to be more frequent. The most commonly affected site was the neck, as in a few other studies [8, 12, 19, 20, 22]. This has been attributed to greater friction by skin to skin contact, collars or necklaces and a tendency to report for visible lesions in the neck region as compared to covered body parts due to cosmetic reasons [23]. Contrary to previous reports which state that ST are common after the age of 40 years [24] and that nearly 60% of individuals acquire ST by the age of 69 years [25], we had a relatively small number of elderly patients. A higher concern about other comorbidities, dependency on family members and financial constraints could be some of the probable reasons. On the other hand, younger age preponderance possibly reflects an increasing awareness, cosmetic concern and urge for treatment of benign conditions too. ST in the majority of patients are asymptomatic; however, 26.78% of our patients had symptoms such as itching, irritation, and pain. Itching has been attributed to increased mast cell counts [5, 23, 26, 27], while irritation and pain may occur because of physical factors such as trauma, friction and/or manipulation.

Skin tags may be associated with several cutaneous and systemic conditions. In our study, 88 (78.57%) patients had one or more associated skin diseases. The commonly noted associations included AN, acne, androgenetic alopecia, hirsutism, and xanthelasma palpebrarum. All of them are associated with metabolic syndrome components [4, 28]. Similarly, we noted systemic conditions such as HT, weight gain or obesity, DM and menstrual irregularity and/or polycystic

**Table 1.** Diagnostic criteria [14–17] for diabetes mellitus, hypertension and dyslipidemia and BMI used in the study**Tabela 1.** Zastosowane w pracy kryteria diagnostyczne [14–17] cukrzycy, nadciśnienia tętniczego, dyslipidemii i wskaźnika masy ciała

Parameter	Fasting plasma glucose [mg/dl]	2-hour post-prandial plasma glucose [mg/dl]
Normal glucose tolerance	< 100	< 140
Prediabetes	100–125	140–199
Diabetes mellitus	≥ 126	≥ 200
Blood pressure	Systolic [mm Hg]	Diastolic [mm Hg]
Normal	< 120	And < 80
Prehypertension	120–139	Or 80–89
Stage 1 hypertension	140–159	Or 90–99
Stage 2 hypertension	≥ 160	Or ≥ 100
Isolated systolic hypertension	≥ 140	And < 90
Lipid profile	Value [mg/dl]	
Total cholesterol:		
Desirable	< 200	
Borderline high	200–239	
High	> 240	
Low-density lipoprotein cholesterol:		
Optimal	< 100	
Near or above optimal	100–129	
Borderline high	130–159	
High	160–189	
Very high	> 190	
High-density lipoprotein cholesterol:		
Low	< 40	
Normal	40–60	
High	> 60	
Triglycerides:		
Normal	< 150	
Borderline-high	150–199	
High	200–499	
Very high	≥ 500	
Body mass index [kg/m <sup>2</sup> ]		
Underweight	< 18.5	
Normal	18.5–24.9	
Overweight	25–29.99	
Obese	≥ 30	
Extremely obese	≥ 40	

**Table 2.** Clinico-epidemiological profile of patients with skin tags with and without metabolic syndrome (MS)**Tabela 2.** Charakterystyka kliniczno-epidemiologiczna pacjentów z włókniami miękkimi z zespołem metabolicznym lub bez zespołu metabolicznego

Parameter	Patients with MS (n = 47)	Patients without MS (n = 65)	P-value
Age group [years]:			
Up to 20	0	3	< 0.0001 <sup>†</sup>
21–30	4	14	
31–40	8	24	
41–50	14	13	
51–60	14	5	
Above 60	7	6	
Gender:			
Male	22	31	0.926
Female	25	34	
Duration:			
< 1 month	1	1	0.196
1–6 months	1	9	
6–12 months	10	13	
> 1 year	35	42	
Distribution of skin tags*:			
Face	11	15	0.967
Neck	45	54	0.038 <sup>†</sup>
Axilla	28	25	0.027 <sup>†</sup>
Chest	6	9	0.868
Abdomen	4	1	0.077
Back	2	3	0.927
Thigh	14	2	< 0.0001 <sup>†</sup>
Others	1	5	0.196
No. of skin tags:			
1	2	6	< 0.0001 <sup>†</sup>
2–5	4	9	
6–10	12	22	
11–20	16	21	
21–30	6	6	
> 30	7	1	
Color of skin tags:			
Skin-colored	20	34	0.586
Hyperpigmented	18	20	
Both	9	11	

Table 2. Cont.

Tabela 2. Cd.

Parameter	Patients with MS (n = 47)	Patients without MS (n = 65)	P-value
Morphology:			
Pedunculated	39	51	0.553
Sessile	0	0	
Both	8	14	
Symptomatology*:			
Irritation	5	10	0.466
Itching	9	4	0.034†
Pain	2	3	0.927
Associated skin disease*:			
Acanthosis nigricans	20	17	0.069
Acne vulgaris	5	11	0.348
Warts	2	5	0.458
Androgenetic alopecia	2	5	0.458
Hirsutism	1	5	0.196
Intertrigo	5	2	0.103
Dermatosis papulosa nigra	1	5	0.196
Xanthelasma palpebrarum	3	0	0.458

\*Some patients had more than one entity, †statistically significant.

ovarian syndrome (PCOS), which have been linked to MS [4]. In the present study, the diagnostic criteria of MS were fulfilled by 47 (41.96%), as observed in a study by Sari *et al.* [3]. However, in other studies [2, 12, 13] a relatively higher occurrence of MS was reported. Analyzing the individual parameters, we found 41.96% and 20.54% of patients to be overweight and obese respectively, which was in accordance with several other studies [3, 12, 19, 23].

An Indian study [29] reported 19% patients with ST to be hypertensive, while in our study the prevalence of HT was higher (33.03%). Abnormal glucose tolerance was observed in 36.6% of our patients, which is close to 40.6% obtained in another Indian study [21]. However, Thappa [30] documented disorders of glucose tolerance in 62.8% of patients. A large proportion of patients in our study were found to have a deranged lipid profile; with increased LDL-C as the most common lipid abnormality, followed by a low HDL-C level. Several studies [2, 3, 8, 12, 20, 22, 29] have linked ST with dyslipidemia. On the other hand, a recent study by Rasi *et al.* [31] found no significant differences between lipid profiles of the normal population and patients with ST.

In this study, a large proportion of patients were found to be prehypertensive and prediabetic. Such

patients are likely to benefit from lifestyle modifications such as dietary changes and physical activity. Since several of our patients with ST were diabetic, hypertensive or dyslipidemic, all such patients should be evaluated for early detection of these complications to start interventions to prevent further serious consequences.

Next, we compared the ST patients with and without MS. We found that the majority of the patients with MS were in the age groups of 41–50 and 51–60 years. Patients with 11 or more ST were more likely to have MS. Shaheen *et al.* [13] had reported that patients fulfilling criteria for MS had a significantly higher number of ST. Akpinar and Dervis found that [12] patients with MS have 11 or more ST in comparison to patients without MS. The site of ST may have some relationship with MS. In our study patients with lesions in the thigh, neck and axilla regions were more likely to have MS; this finding was not observed in previous studies. However, Sari *et al.* [3] reported that the number and distribution of ST were not related to other parameters.

The presence of AN, which is regarded as a marker of insulin resistance [32], was not found to be significantly different in patients with and without MS. No statistically significant difference was noted

**Table 3.** Investigative findings of patients ( $n = 112$ ) with skin tags  
**Tabela 3.** Wyniki badań dodatkowych u 112 chorych z włóknikami miękkimi

Parameter	No. of patients
Blood glucose level:	
Normal	71
Impaired glucose tolerance	22
Diabetes mellitus	19
Total cholesterol:	
Desirable	77
Borderline high	23
High	12
Triglyceride:	
Normal	74
Borderline high	25
High	11
Very high	2
High-density lipoprotein cholesterol:	
Normal	62
Low	47
High	3
Low-density lipoprotein cholesterol:	
Optimal	48
Near or above optimal	35
Borderline high	19
High	7
Very high	3
Very low-density lipoprotein:	
Normal	76
High	36

in patients with and without MS regarding duration, color or morphology of ST.

## CONCLUSIONS

Patients with ST should be screened for concomitant diseases such as diabetes, hypertension, dyslipidemia and cardiovascular diseases. Patients with 11 or more skin tags and involvement of the thighs have a high possibility of underlying metabolic syndrome. Younger patients usually report early, on account of their cosmetic concern, thereby providing an opportunity to screen them for metabolic syndrome.

me. Early detection of these complications followed by appropriate lifestyle modifications and/or drug therapy would be beneficial in terms of reducing the considerable morbidity and mortality.

## Conflict of interest

The authors declare no conflict of interest.

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