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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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.

KEY WORDS: skin tags, metabolic syndrome, acanthosis nigricans, insulin resistance.

SŁOWA KLUCZOWE: włókniaki miękkie, zespół metaboliczny, rogowacenie ciemne, insulinoporność.

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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.
**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.

**OBJECTIVE**

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

**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.
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)/height² (in m²), 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 h-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 χ² 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 ≥ 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

| 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/m²]**

|                   |                |
|-------------------|----------------|
| 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 włókniakami 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† |
| 21–30 | 4 | 14 | |
| 31–40 | 8 | 24 | |
| 41–50 | 14 | 13 | |
| 51–60 | 14 | 5 | |
| Above 60 | 7 | 6 | |
| Gender: | | | 0.926 |
| Male | 22 | 31 | |
| Female | 25 | 34 | |
| Duration: | | | 0.196 |
| < 1 month | 1 | 1 | |
| 1–6 months | 1 | 9 | |
| 6–12 months | 10 | 13 | |
| > 1 year | 35 | 42 | |
| Distribution of skin tags*: | | | 0.967 |
| Face | 11 | 15 | |
| Neck | 45 | 54 | 0.038† |
| Axilla | 28 | 25 | 0.027† |
| Chest | 6 | 9 | 0.868 |
| Abdomen | 4 | 1 | 0.077 |
| Back | 2 | 3 | 0.927 |
| Thigh | 14 | 2 | < 0.0001† |
| Others | 1 | 5 | 0.196 |
| No. of skin tags: | | | < 0.0001† |
| 1 | 2 | 6 | |
| 2–5 | 4 | 9 | |
| 6–10 | 12 | 22 | |
| 11–20 | 16 | 21 | |
| 21–30 | 6 | 6 | |
| > 30 | 7 | 1 | |
| Color of skin tags: | | | 0.586 |
| Skin-colored | 20 | 34 | |
| Hyperpigmented | 18 | 20 | |
| Both | 9 | 11 | |
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 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

| 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. 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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