

Significance of Acanthosis Nigricans as Marker for Metabolic Syndrome

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Abstract: Metabolic syndrome refers to a clustering of metabolic risk factors including central obesity, glucose intolerance, hyperinsulinemia, low HDL cholesterol, high triglycerides and hypertension. MS is increasingly being recognized as a risk factor for cardiovascular disease and cardiovascular mortality. Lipoatrophy, acanthosis nigricans is a skin markers associated with this syndrome. Acanthosis nigricans is a brown to black, poorly defined, velvety hyperpigmentation of the skin. It is usually found in body folds, such as the posterior and lateral folds of the neck, the axilla, groin, umbilicus, forehead. It is associated with obesity, endocrinopathies, internal malignancies. The most common cause of acanthosis nigricans is insulin resistance, which leads to increased circulating insulin levels. Insulin spillover into the skin results in its abnormal increase in growth This work was carried out to find out specificity and sensitivity of acanthosis nigricans as skin marker for metabolic syndrome. This study is a cross sectional study. Male and female patients of age > 20 years were selected. exclusion criteria: History of Diabetes mellitus, Hypertension, Dyslipidemia, Pregnant women, smoking, alcohol study sample size 100. Patients Waist circumference, Fasting blood sugar and lipids, blood pressure were investigated. Acanthosis nigricans was looked for in all patients. *Result:* that S30 out of 48 patients who tested positive for metabolic syndrome had acanthosis. Sensitivity and specificity were 62.50% and 94.23% In conclusion Acanthosis nigricans as a marker for metabolic syndrome has high specificity and good sensitivity.

Key words: Metabolic syndrome (MS) • Acanthosis nigricans • Dyslipidemia • Hypertension • Waist circumference • Diabetes mellitus

INTRODUCTION

Metabolic syndrome refers to a clustering of metabolic risk factors including central obesity, glucose intolerance, hyperinsulinemia, low hdl Cholesterol, high triglycerides and hypertension. People with MS are twice as likely to die from and three times as likely to develop, myocardial infarction or stroke compared to people without MS. They also have a five-fold greater risk of developing type 2 diabetes (if not already present). Metabolic syndrome is increasingly being recognized as a risk factor for cardiovascular disease and cardiovascular mortality [1].

It is estimated that approximately 25% of the world's population has metabolic syndrome. Individuals that are genetically predisposed to insulin resistance combined

with physical inactivity and obesity can elicit insulin resistance and the progression to metabolic syndrome. the world health organisation proposed a definition of ms in 1999 and the national cholesterol education program expert panel and adult treatment panel iii published a working definition in 2001. The us national cholesterol education program adult treatment panel iii (2001) requires at least three of the following [2].

- Central obesity: waist circumference \geq 102 cm or 40 inches (male), \geq 88 cm or 36 inches (female)
- Dyslipidemia: tg \geq 1.7 mmol/l (150 mg/dl)
- Dyslipidemia: hdl-c $<$ 40 mg/dl (male), $<$ 50 mg/dl (female)
- Blood pressure \geq 130/85 mmhg
- Fasting plasma glucose \geq 6.1 mmol/l (110 mg/dl)

The metabolic syndrome is typically not associated with symptoms. On physical examination, waist circumference may be expanded and blood pressure elevated. The presence of one or either of these signs should alert the clinician to search for other biochemical abnormalities that may be associated with the metabolic syndrome.

Lipoatrophy, acanthosis nigricans, skin tags, psoriasis are common skin markers associated with this syndrome. Because these physical findings typically are associated with severe insulin resistance, other components of the metabolic syndrome should be expected.

Acanthosis Nigricans: It is a brown to black, poorly defined, velvety hyperpigmentation of the skin. It is usually found in body folds [3] such as the posterior and lateral folds of the neck, the axilla, groin, umbilicus, forehead and other areas.

Causes: It typically occurs in individuals younger than age 40, may be genetically inherited and is associated with obesity or endocrinopathies, such as: hypothyroidism or hyperthyroidism, acromegaly, polycystic ovary disease, insulin-resistant diabetes, or cushing's disease.

Endocrine: The most common cause of acanthosis nigricans is insulin resistance, which leads to increased circulating insulin levels. Insulin spillover into the skin results in its abnormal increase in growth (hyperplasia of the skin). The condition most commonly associated with insulin resistance is type 2 diabetes mellitus, but is also a prominent feature of obesity, polycystic ovary syndrome, donohue syndrome and rabson-mendenhall syndrome. Acanthosis nigricans may also be seen with certain medications that lead to elevated insulin levels (e.g., glucocorticoids, niacin, insulin, oral contraceptives and protease inhibitors) [4].

Malignant: In the context of a malignant disease, acanthosis nigricans is a paraneoplastic syndrome and is then commonly referred to as acanthosis nigricans maligna. Involvement of mucous membranes is rare and suggests a coexisting malignant condition [5].

When seen in individuals older than age 40, this disorder is commonly associated with an internal

malignancy, usually adenocarcinoma and most commonly of the gi tract or uterus; less commonly of the lung, prostate, breast, or ovary. The stomach is the most common site [6]. Acanthosis nigricans of the oral mucosa or tongue is highly suggestive of a neoplasm, especially of the gi tract.

Other Causes: Familial, drug-induced and idiopathic.

Types: Classification of acanthosis nigricans according to schwartz, 1994 [2] [7, 8].

- Benign acanthosis nigricans
- Acanthosis nigricans associated with obesity
- Syndromic acanthosis nigricans
- Malignant acanthosis nigricans
- Acral acanthosis nigricans
- Unilateral acanthosis nigricans
- Drug-induced acanthosis nigricans
- Mixed acanthosis nigricans

Other Classifications of Acanthosis Nigricans: Acanthosis nigricans may also be divided into the following types [1]: 506:

- Acral acanthotic anomaly (acral acanthosis nigricans)
- Acanthosis nigricans type i
- Acanthosis nigricans type ii
- Acanthosis nigricans type iii

Treatment: Topical medications like keratolytics - topical tretinoin, 0.05%, ammonium lactate 12% cream, depigmenting cream with sunscreen lotion, calcipotriol, urea, salicylic acid have been used. Oral agents- etretinate, isotretinoin, metformin, dietary fish oils. Dermabrasion and long pulsed alexandrite laser therapy may be used to reduce the bulk of the lesion. People with acanthosis nigricans should be screened for diabetes and, although rare, cancer. Controlling blood glucose levels through exercise and diet often improves symptoms. Acanthosis nigricans maligna may resolve if the causative tumor is successfully removed.

Prognosis: Acanthosis nigricans often fades if the underlying cause can be determined and treated appropriately.



Aim of the Study: To find out specificity and sensitivity of acanthosis nigricans as skin marker for metabolic syndrome. This study is a cross sectional study.

Inclusion Criteria: Male and female patients of age > 20 years were selected.

Exclusion Criteria:

- History of diabetes mellitus
- History of hypertension
- History of dyslipidemia
- Pregnant women
- History of smoking
- History of alcohol
- Patient who is not willing to participate in the study
- Individuals who are cognitively impaired
- Any other health or mental condition that in the investigator's opinion may

Adversely affect the subject's ability to complete the study.

Description of the Study

Study Sample Size 100: Patients satisfying the criteria for our study were briefed about the study intention and consent obtained for collecting blood samples and taking measurements.

Basic demographic data collected. Patient's waist circumference, fasting blood sugar and lipids, blood pressure were collected. Acanthosis nigricans was looked for in all patients.

RESULTS

Sensitivity Analysis: 30 out of 48 patients who tested positive for metabolic syndrome had acanthosis.

Acanthosis	Metabolic syndrome		Total
	Yes	No	
Yes	30	3	33
No	18	49	67
Total	48	52	100

Parameter	Estimate	Lower - upper 95% cis
Sensitivity	62.50%	(48.36, 74.78)
Specificity	94.23%	(84.36, 98.02)
positive predictive value	90.91%	(76.43, 96.86)
negative predictive value	73.13%	(61.48, 82.28)
diagnostic accuracy	79.00%	(70.02, 85.83)

CONCLUSION

- Acanthosis nigricans as a marker for metabolic syndrome has high specificity and good sensitivity.
- If identified, patients can be screened for metabolic syndrome and treated early to prevent morbidity and mortality related to cardiovascular risk.

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