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Research Paper

A Study on Clinico-Aetiological Profile of Acanthosis Nigricans in a Rural Medical College

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Introduction

Acanthosis Nigricans is characterised by darkening (hyper pigmentation) and thickening (hyperkeratosis) of the skin, occurring mainly in the folds of the skin in the armpit (axilla), groin and back of the neck. It can occur with endocrine diseases such as diabetes mellitus, thyroid disorders, Cushing disease, PCOD, underlying malignancies, certain drugs, and as a genetic disorder. It is most common in people who have insulin resistance those whose body is not responding correctly to the insulin that they make in their pancreas. It is not a skin disease per se but a cutaneous sign of an underlying disorder.

Neck is the most commonly affected area. More than ninety percent of peoples AN have neck involvement. Axilla is the second most common area involved. There are two important types of acanthosis nigricans: benign and malignant. Although it is classically described as a sign of internal malignancy, this is very rare. Benign types, sometimes described as 'pseudoacanthosis nigricans' are much more common which is related to obesity. AN is common in some populations and its prevalence changes with different races and is more prevalent in people with darker skin pigmentation.

Acanthosis nigricans (AN) is a dermatosis characterized by velvety, papillomatous, brownish-black, hyperkeratotic plaques, typically appears on the intertriginous areas and neck. A although it may be associated with internal malignancy, it is more common with obesity and insulin resistance and hence allows for diagnosis of related disorders including type 2 diabetes, the metabolic syndrome, and polycystic ovary syndrome in asymptomatic cases also. Early recognition of these conditions is very helpful for prevention of disease progression and related complications. The exact incidence of acanthosis nigricans is unknown. In a study of unselected population of 1412 children, the changes of AN were present in 7.1%.

Need of the study

Acanthosis nigricans is a common skin condition which may affect all age group and the list of underlying cause is extensive ranging from a simple benign familial type through syndromic to malignant cause. Clinician should be aware of this and have to find out the underlying condition and

patient should be managed appropriately at the earliest.

Aims

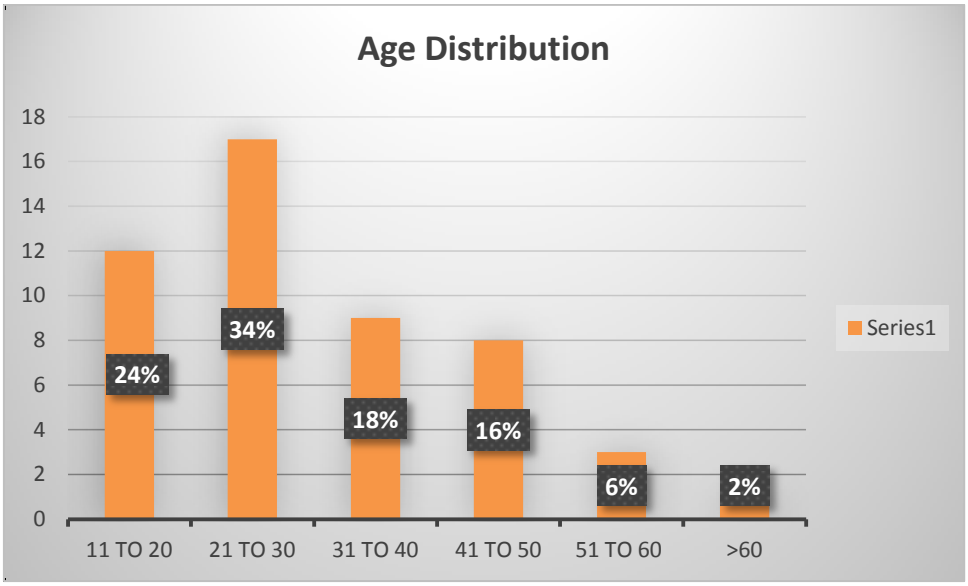
1. To evaluate the clinical features and epidemiology of acanthosis nigricans
2. To find out the common disorders associated with acanthosis nigricans.

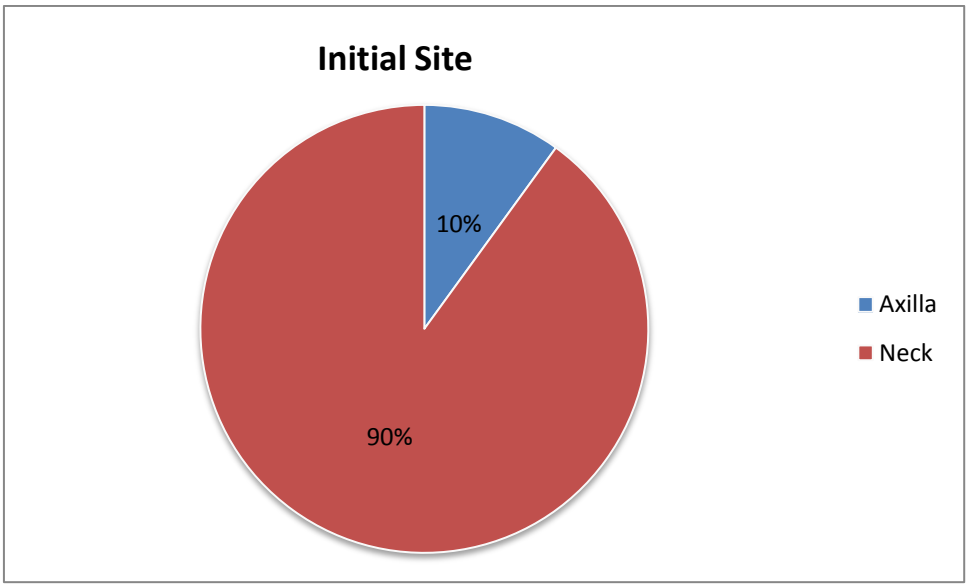
Materials and Methods

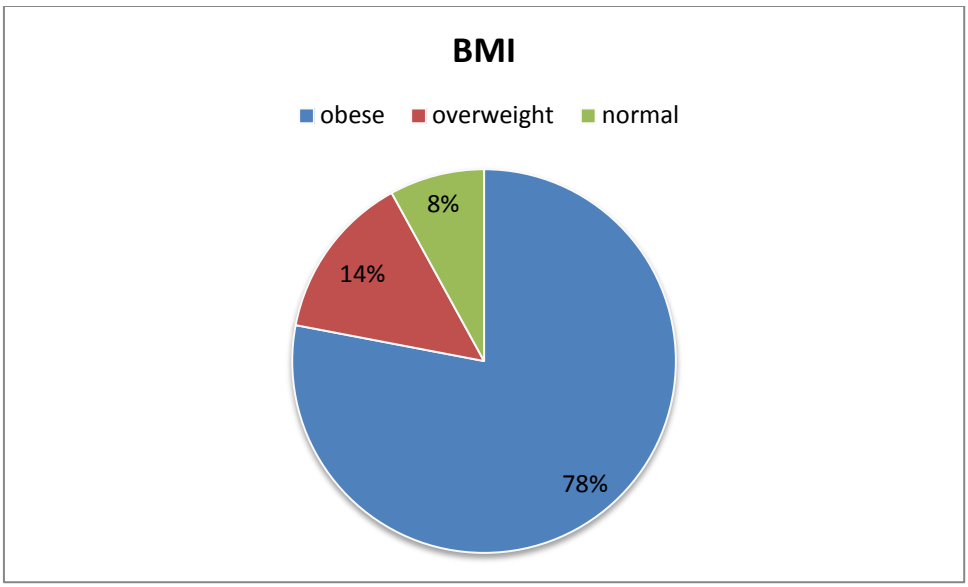
50 patients are selected for this study. Prior approval of hospital research committee and ethical committee was obtained. We selected 50 patients having acanthosis nigricans. Biodata collected. Detailed history taken. All patients were underwent thorough clinical examination including weight and the height.BMI calculated for each patient. All patients had AN with velvety, hyper pigmented thickening of skin. Most of the patient had AN over nape of neck Papillomatous formation was present in most cases. No eyelids, conjunctiva or oral cavity involvement with AN was found in any of the patients in this study. All patients were subjected to blood investigations including complete blood count, s.creatinine, LFT, FBS, PPBS, Fasting lipid profile, hormone measurements by radioimmunoassays of thyroid function tests, free testosterone, LH, FSH & cortisol and USG abdomen and pelvis to find out underlying disease or condition. Obesity was diagnosed when BMI exceeded 24 kg/m^2. Diabetes mellitus is diagnosed with a fasting blood sugar≥ 126mg/dl and post prandial blood sugar ≥200mg/dl. Following criteria was considered in diagnosing PCOS 1) history of menstrual irregularities and/or anovulation; 2) hirsutism and/acne; 3) elevated serum-free testosterone and/or elevated luteinizing hormone/follicle-stimulating hormone (LH/FSH) ratio; and 4) ultrasonographic finding of polycystic ovaries. Diabetes mellitus is diagnosed with a fasting blood sugar≥ 126mg/dl and post prandial blood sugar ≥200mg/dl.

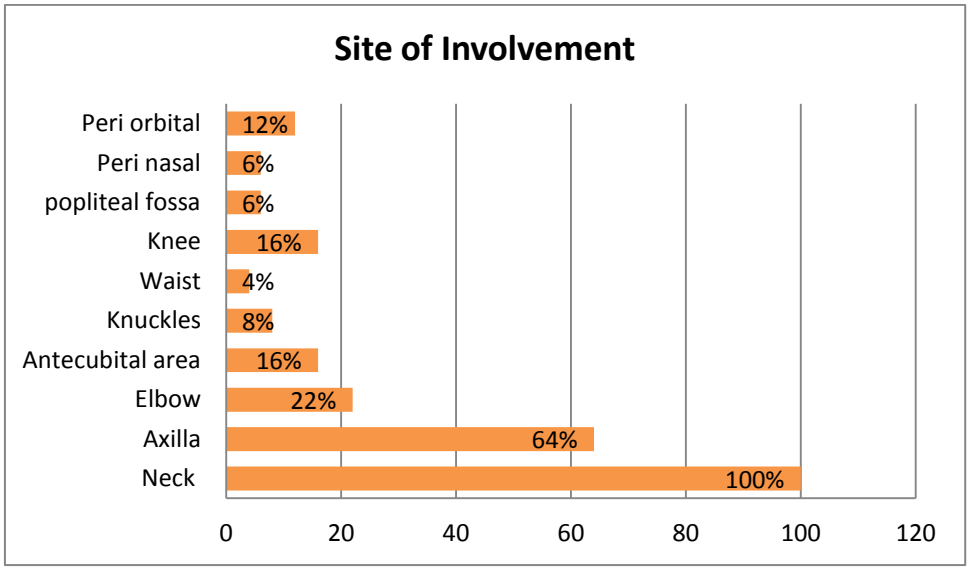
Results and Observation

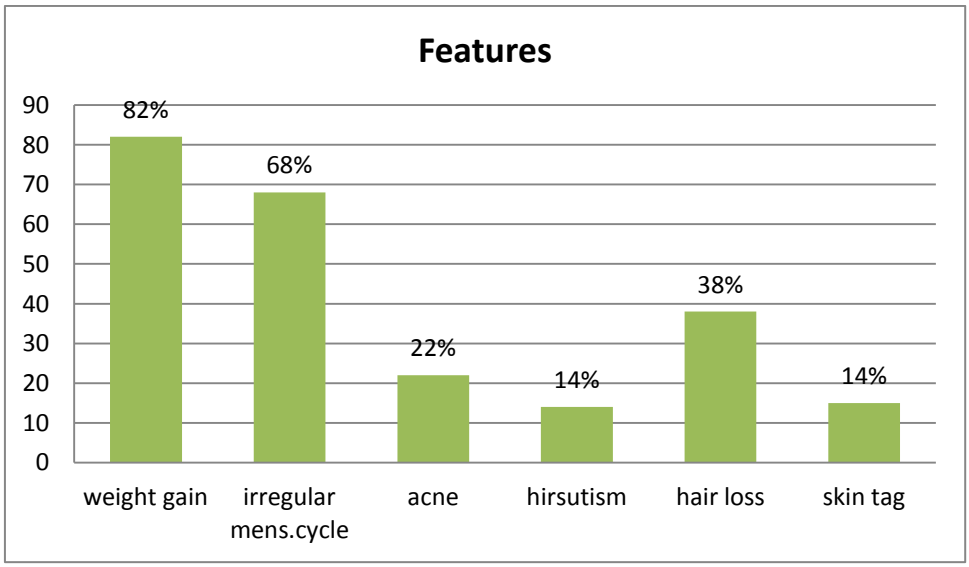
This study conducted with 50 patients with acanthosis nigricans. It is clear that females are outnumbered to males with 47 females and 3 males. Most common age group affected with AN in this study is21- 30 years with 34% patients and another24 % patients were between 11- 20 years and 2% patients were more than 60 years of age. In our study 44% of patients having diabetes mellitus history and 14% patients have hypothyroidism and another 4% patients have hyperthyroidism.26% of patients have family history polycystic ovarian syndrome. Another important finding is 66% of patients give family history of diabetes mellitus. All patients complaints of darkening of body parts and 82% of patients have weight gain. Neck is the most common initial site of presentation with 90% of patients. 68% patients gave the history of irregular menstrual cycles and rest of the female patients have regular cycles. 22% of patients complained of acne and 14% of patients have hirsutism. 38% patients have hair loss and 10% have skin tag. This study showed that , 78% patients have BMI in obesity range and, 14 % patients BMI in overweight range and 8% of patients have BMI in normal range. Maximum BMI noted in this study is 37.6. The commonest site of acanthosis nigricansis neck with involvement in 100% of patients, followed by axilla in 64% patients, elbow 22%, anti-cubital fossa 16%, knuckles 8% and knees 8%. Few patients showed involvement of periorbital, perinasal, waist region involvement also.40% patients have high fasting and post prandial blood sugar level showing uncontrolled diabetes mellitus. Ultrasound abdomen and pelvis showed 56% patients have features of PCOD, 14% patients have medical renal disease and rest of them(30%) having normal study. serum testosterone levels were elevated in 18% patients and increased dehydroepiandrosterone sulphate (DHEAS) levels were seen in 12% patients.


Age Distribution
18
16
14
12
10
8
6
4
2
0
24%
34%
18%
16%
6%
2%
11 TO 20
21 TO 30
31 TO 40
41 TO 50
51 TO 60
>60
Series1


Initial Site
10%
90%
Axilla
Neck


BMI
obese
overweight
normal
8%
14%
78%





Discussion

Acanthosis nigricans is characterized by dark, coarse, thickened skin with a velvety texture and most commonly seen in skin folds. It is usually asymptomatic or minimal pruritis. Clinical hallmark of AN is appearance dark/ grey brown velvety plaques which most initially appears over neck or axilla. It is also seen in eyelids, peri-nasal area, lips, vulva, mucosal surfaces, dorsal hands, and flexural areas in the groin, knees, elbow and umbilical region. Neck is the most commonly affected area. More than ninety percent of peoples AN have neck involvement. Axilla is the second most common area involved. 5 anatomical sites have chosen to assess the presence and extend of acanthosis nigricans. These include neck, axilla, knuckles, elbows and knees. There are two types of acanthosis nigricans: malignant AN and benign AN. The lesions of malignant and benign acanthosis nigricans are indistinguishable.

Acanthosis nigricans is a common skin condition and is a marker of many conditions like insulin resistance, internal malignancy, etc. The exact etiology is not defined. Several possibilities are suggested. There are multiple factors involved in the development of acanthosis nigricans.

- Increased circulating insulin that activates keratinocyte insulin-like growth factor (ILGF) receptors, particularly IGF-1. At high concentrations, insulin may displace IGF-1 from IGF binding protein. Increased circulating IGF may lead to keratinocyte and dermal fibroblast proliferation.

- Hereditary variants are associated with fibroblast growth factor defects.
- Increased transforming growth factor (TGF) appears to be the mechanism for malignancy-associated acanthosis nigricans. TGF acts on epidermal tissue via the epidermal growth factor receptor.

There are nine types of acanthosis nigricans based on etiology. 1.Obesity associated AN 2.Syndromic AN 3.Acral AN 4.Unilateral AN 5.Generalized AN 6.Familial AN 8.Drug induced AN 8.Malignant AN 9.Mixed type AN.

Obesity assocated Acanthosis nigricans is most common type and it is also called as pseudo acanthosis nigricans. It is seen in 70% patients and it appears usually in middle age individuals. It is weight dependent and and associated with insulin resistance. More than half the adults who weigh greater than 200% of their ideal body weight have lesions consistent with AN. Weight reduction leads to almost complete regression of lesions. syndromic AN is second most common and it is reported in 23.35% patients with acantosis nigricans. Type A and type B are two important examples. Type A syndrome comprised of hyperandrogenemia, insulin resistance, acanthosis nigricans syndrome (HAIR AN syndrome) and it is seen in young women and may be familial also. polycystic ovaries and high testosterone are common with this type of AN. Type B is usually seen in women with uncontrolled diabetes mellitus, ovarian hyperandrogenism and/or any autoimmune disease like SLE, hashimotos thyroiditis, sjogrens syndrome. Drug-induced AN is an uncommon type, may be associated with exposure to many drugs including systemic corticosteroids, nicotinic acid, insulin, oral contraceptives, pituitary extract, diethylstilbestrol. triazinate, fusidic acid, and methyltestosterone. The lesions of AN may regress completely following withdrawal of the offending drugs. Malignant AN may be associated with any types of malignancy. The most frequent incidence of acanthosis nigricans were with adenocarcinomas of the gastrointestinal tract (70-90%), particularly gastric cancer (55-61% of malignant AN cases). Reappearance of acanthoosis nigricans in the setting of a treated internal malignanacy may suggest recurrence or metastasis of the primary tumor.

Most of the patients are asymptomatic except cosmetic concern and present with a thickened dark area of asymptomatic area of skin. Some may present with pruritus. Lesions may begin as hyperpigmented macules and patches and later on progress to palpable plaques.

Some patients with malignant acanthosis nigricans, patients present with skin changes of acanthosis nigricans before any signs of cancer. In some other patients, the lesions of acanthosis nigricans develop simultaneously with the neoplasm. In the remaining cases, the skin findings may not be evident or manifest after the diagnosis of cancer. Malignant acanthosis nigricans has higher incidence of pruritis.

For patient with skin lesion suggestive of acanthosis nigricans, patient is to be evaluated to find out the underlying cause. Workup for Insulin resistance and internal malignanacy are important. Diabetes mellitus can be ruled out by glycosylated haemogloin or glucose tolerance test. Insulin resistance can be screened by plasma insulin level, which will be high in patients with insulin resistance. Skin biopsy and histological examination may be useful in diagnosis of acanthosis nigricans. Hyperkeratosis, papillomatosis, with minimal or no acanthosis or hyper pigmentation are main histological features of acanthosis nigricans. Biopsy and histopathological study may show thickened stratum corneum with minimal involvement of the dermis except for thickened and elongated dermal projections. The dark color of AN is mostly due to hyperkeratosis but a mild increase in melanin pigmentation also contributes.. Tissue staining with colloidal iron often shows infiltration of the papillary dermis with glycosaminoglycans such as hyaluronic acid, particularly in patients with

gonadal disease such as polycystic ovarian syndrome (PCOS).

There is no treatment of choice for acanthosis nigricans. Treatment of underlying cause is the mainstay in the management of acanthosis nigricans. Skin lesions are treated for cosmetic reasons only. Treatment for hyperinsulinaemia and diabetes, weight reduction in obesity, cessation of offending agent in drug induced AN, treatment for thyroid disorders, improvement of lipid profile, correction of menstrual irregularity, all may result in resolution of dermatosis.

Topical medications may be effective in some cases of AN include keratolytics (e.g.,ammonium lactate 12% cream, topical tretinoin 0.05%, or a combination of the two) and triple-combination depigmenting cream (tretinoin 0.05%, hydroquinone 4%, fluocinoloneacetonide 0.01%) nightly with daily sunscreen. Other drugs include Calcipotriol, podophyllin, urea, and salicylic acid also have been tried with variable results.

Systemic agents which have proven some benefits in acanthosis nigricans include metformin, oral contraceptive agents, isotretinoin, etretinate, dietary fish oils, octreotide in different groups of people with acanthosis nigricans. Dermabrasion and laser therapy may also be tried if cosmetically indicated. Surgical removal of tumors is the mainstay of treatment for malignant acanthosis nigricans. Cyproheptadine can be tried in malignant acanthosis nigricans.

Conclusion

Acanthosis nigricans is commonly associated with insulin resistance and metabolic syndrome although it may be rarely an external sign of internal malignanacy. Mostly it is asymptomatic other than cosmetic issue. Earlier workup of acanthosis nigricans will be helpful for early treatment of underlying cause and prevention of complications.

References

1. Fine RM. Acanthosis nigricans. Int J Dermatol.
2. Brown J, Winkelmann RK. *Acanthosis nigricans*: A study of 90 cases. Medicine (Baltimore)
3. Barbieri RL, Ryan KJ. Hyperandrogenism, insulin resistance, and *acanthosis nigricans* syndrome: A common endocrinopathy with distinct pathophysiologic features. Am J Obstet Gynecol.
4. Grasinger CC, Wild RA, Parker IJ. Vulvar achanthosis nigricans: A marker for insulin resistance in hirsute women. FertilSteril.
5. Curth HO. *Acanthosis nigricans*: birth defects. Orig Art Ser.
6. Annos T, Taymor ML. Ovarian pathology associated with insulin resistance and *acanthosis nigricans*. Obstet Gynecol.
7. Conway GS, Jacobs HS. Clinical implications of hyperinsulinemia in women. Clin Endocrinol (Oxf) 12. Higgins SP, Freemark M, Prose NS. *Acanthosis nigricans*: a practical approach to evaluation and management. Dermatol Online J.
8. Imperato-McGinley J, Peterson RE, Sturla E, Dawood Y, Bar RS. Primary amenorrhea, associated with hirsutism, *acanthosis nigricans*, dermoid cysts of the ovaries and a new type of insulin resistance. Am J Med.
9. Flier JS, Fastman RC, Minakes KL, Matteson D, Rowe JW. *Acanthosis nigricans* in obese women with hyperandrogenism: Characterization of an insulin-resistant state distinct from the type A and B syndromes. Diabetes. 1985;34:101–7. [PubMed: 3881301]
10. Hud JA, Cohen JB, Wagner JM, Cruz PD. Prevalence and significance of acanthosis nigricans in an adult obese population. Arch Dermatol. 1992;128:941–4. [PubMed: 1626961].