REVIEW ARTICLE

An Indian Expert Group Review of Acanthosis Nigricans with Recommendations for Early Detection and Timely Management

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Abstract

Introduction: Acanthosis nigricans (AN) is a visible cutaneous manifestation of several underlying systemic conditions, such as prediabetes, diabetes mellitus (DM), polycystic ovarian syndrome (PCOS), metabolic syndrome (MS), and malignancy. AN is commonly seen in obese individuals and is a proven skin marker of insulin resistance (IR). Its typical clinical presentation and location, especially on the nape of the neck, allows for easy visual identification. Obesity, IR, and other noncommunicable diseases (NCD) are on the rise in India, with many cases being undiagnosed or missed. Every sixth diabetic in the world is Indian. AN can thus play a vital role in screening, early identification, and reduction of morbidity, especially of IR-related disorders. Currently, there are no national or international multidisciplinary guidelines or recommendations for AN.

Objective: To review published current literature and evidence on AN, its associations, and management. To recommend an approach to clinical identification of AN, associated/underlying disorders, investigations, and management, including lifestyle modifications. To sensitize and familiarize clinicians and healthcare workers across India with AN presentations. This will enable early detection of conditions such as IR, prediabetes, DM, PCOS, malignancy, etc., in practice and in the community.

Materials and methods: The PCOS Society of India constituted a multispecialty Expert Working Group with representation from various national societies to review all published scientific evidence. Expert group meetings were conducted to provide recommendations.

Conclusion: Acanthosis nigricans is a simple, non-invasive, cost-effective screening tool for early identification of IR. It is important to integrate and disseminate information and training on AN across medical specialties. The government of India has launched several National Health Programmes to help address the rising burden of NCD in the population. AN would provide a simple screening tool to pick up undiagnosed or missed cases.

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Introduction

Acanthosis nigricans (AN) is characterized by dark, thickened skin with a velvety texture in a symmetrical distribution on the neck, axillae, antecubital and popliteal fossae, and groins [international classification of diseases-10 (ICD-10), L.83; ICD-11 ED51.0].[1] AN has multiple causes (Table 1); however, benign AN is typically related to high concentrations of insulin, which binds to insulin-like growth factor receptors, leading to epidermal skin cell proliferation.[2] Thus, AN is often a visible cutaneous sign of insulin resistance (IR) (Table 2).

The global prevalence of AN varies from 7 to 74%. The prevalence of AN varies among different ethnic groups. AN appears to be especially prevalent among Asians and individuals of mixed ancestry. A possible genetic predisposition or increased sensitivity of the skin to hyperinsulinemia among certain populations is reported.[3,4] It continues to rise due to an increase in noncommunicable diseases (NCDs) including polycystic ovarian syndrome (PCOS), diabetes mellitus (DM), and metabolic syndrome (MS) in the general population.[6] It is known that IR precedes diabetes by approximately 10–15 years.[7] The presence of AN on physical examination is a reliable marker of IR.[8] Hence, it has been proposed as a simple, noninvasive, cost-effective tool for screening and diagnosis of underlying chronic metabolic disorders such as prediabetes, DM, and MS.[6]

Given the association of AN with DM and obesity, the American Diabetes Association (ADA) has included AN as an indicator of DM risk in overweight youth entering puberty.[9]

Recognizing the higher risk for NCDs specifically in Indians, early detection of AN as a marker of IR is of immense importance.[10,11] Currently, it is an underutilized practical tool. The goal for managing AN is to treat its primary cause, bring about cosmetic resolution of AN lesions, reduce morbidity with timely treatment, and improve the quality of life. Thus, the management of AN needs an interdisciplinary, structured, and systematic approach. Currently, there are no international or national guidelines that address a multidisciplinary approach for AN. We present an evidence-based review and propose expert recommendations for early detection, treatment, and preventive management in the Indian setting.

Materials and Methods

The PCOS Society of India identified AN as a priority area and constituted a multidisciplinary Expert Working Group (Table 3) for review and recommendations.

A detailed review of the literature was performed using PubMed and Google Scholar using the main keywords such as "acanthosis nigricans," "insulin resistance," and "PCOS." Publications available in the English language were included in the final review. The references were classified as per the available evidence as level 1–5, with level 1 being the highest evidence (randomized controlled trial/meta-analysis) and level 5 being the lowest (case report). Expert group meetings were conducted to deliberate on the recommendations for early detection of AN, prevention, and management of AN-associated disorders in the Indian context.

Clinical Features and Diagnosis

Clinical Features of Acanthosis Nigricans

The typical clinical appearance of AN allows for easy diagnosis.[12] AN can sometimes be

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Table 1: Acanthosis nigricans and causes[2]

Causes	*Forms of AN*
Metabolic disorders	Obesity-associated AN • Most common form of AN, associated with IR • Severity of lesions related to the amount of weight excess Syndromic type A and B • Type A (HAIR-AN): AN with IR, hyperandrogenemia • Type B: AN, DM, ovarian hyperandrogenemia
Genetic disorders	Unilateral AN • Linear, unilateral variant, similar to classical AN • Manifests during childhood or later Familial AN • Rare autosomal dominant disease in early childhood • Self-limited, stabilizes or recedes postpuberty Benign genetic AN • Develops from birth or early childhood as a rare autosomal dominant form
Autoimmune	AN associated with autoimmune disease • Anti-IR antibodies in autoimmune diseases (e.g., SLE) AN only with autoantibodies
Paraneoplastic AN	AN associated with neoplasia • Rapid onset, sudden and intensely pruritic lesions • Usually associated with adenocarcinomas of abdominal organs and genitourinary cancers • Precedes, accompanies, or follows diagnosis of internal cancer
Iatrogenic AN	• Adverse effect of certain drugs, for example, insulin, niacinamide, oral corticosteroids, oral contraceptives, aripiprazole, somatotropin, diethylstilbestrol, testosterone, pituitary extract of β-MSH, triazinate, amprenavir, palifermin, fusidic acid • Lesions usually reversible on discontinuation of drug
Idiopathic AN	• Acral AN • Limited to dorsal surfaces of hands and feet (less to elbows, knees, knuckles)
Mixed type AN	• AN lesions with any two forms of AN from above

Table 2: What is IR?[5]

- IR is an impaired biologic response to insulin stimulation of target tissues (liver, muscle, and adipose tissue)
- IR impairs glucose disposal, resulting in a compensatory increase in beta-cell insulin production and hyperinsulinemia
- Till date the clinical definition of IR remains elusive
- Clinically, IR is recognized by the metabolic consequences associated with it, namely MS and IR Syndrome

Table 3: Acanthosis nigricans Expert Working Group

- PCOS Society of India in collaboration with the following:
  - Association of Physicians of India (API)
  - Endocrine Society of India
  - Experts from Sports/Fitness medicine
  - Indian Academy of Pediatrics (IAP)
  - Indian Association of Dermatologists Venereologists and Leprologists (IADVL)
  - Indian College of Obstetricians &Gynaecologists (ICOG)
  - ICMR-National Institute for Research in Reproductive and Child Health (ICMR-NIRRCH)
  - Indian Dietetics Association
  - Indian Society of Medical and Pediatric Oncology (ISMPO)
  - Medical Research Centre-Kasturba Health Society
  - Mumbai Obstetrics and Gynecological Society (MOGS)
  - Sir Vithaldas Thackersey College of Home Science (Autonomous), SNDT Women's University
  - Tata Institute of Social Sciences (TISS)

pruritic, associated with skin tags, or present at atypical sites including the face, knuckles, etc. (Fig. 1). Burke et al. have developed a validated, quantitative scale (Table 4) to measure the severity of AN lesions appearing on various body parts.[13]

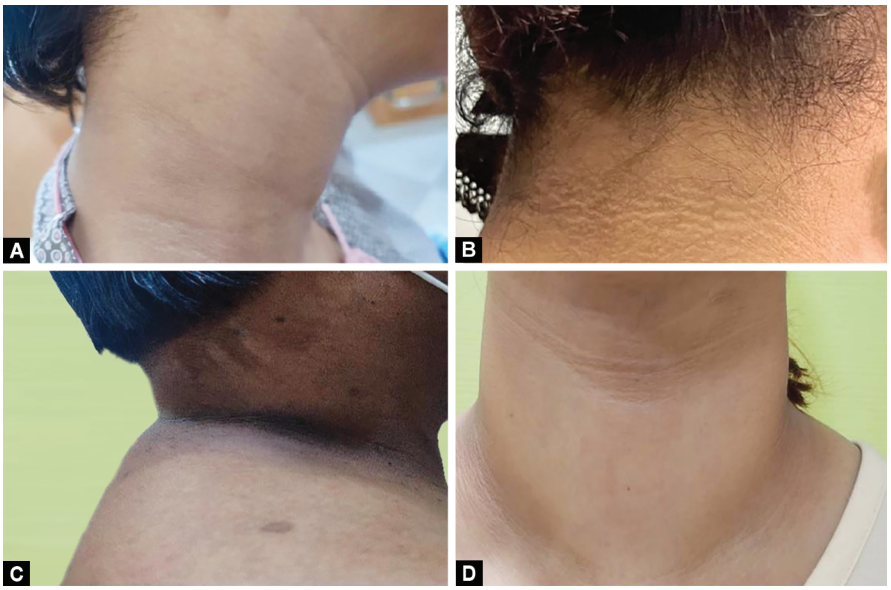
Recommendation 1: Acanthosis nigricans can be suspected from general skin examination due to its classical clinical appearance on typical sites.

Diagnosis of Acanthosis Nigricans

Clinical examination is usually sufficient to diagnose AN as the clinical picture is quite characteristic. Clinicians can rule out dermatitis neglecta (accumulation of dirt on the skin) by wiping the skin with an alcohol swab. For other differentials, a dermatologist can be consulted. Rarely, a skin biopsy may be required.

Dermoscopy

It is a skin magnification test done using a dermatoscope, not commonly performed in



Figs 1A to D: Clinical grades of AN (Burke's scale); Courtesy: Dr Gulrez Tyebkhan, Saifee Hospital, Mumbai; Grade 1: Present; Grade 2: Mild; Grade 3: Moderate; and Grade 4: Severe

clinical practice and requires special training. Features are detailed in Figure 2.[14]

Acanthosis Nigricans, Insulin Resistance and Associated Conditions

Prevalence

Insulin resistance syndrome (IRS) is a manifestation of excess insulin and variable resistance to its action. Features include hyperglycemia, hypertension, dyslipidemia, visceral adiposity, and hyperuricemia. Elevation of inflammatory markers, endothelial dysfunction, and a prothrombotic state are also observed. Table 5 provides the reported prevalence of AN with the associated conditions in adults and children.

Prospective analysis of plasma insulin levels in healthy normoglycemic male (19–73 years) and female (19–55 years) volunteers are reported. Reference range for insulin in a

Table 4: Burke's scale for AN[13]

Location and score	*Description*
Neck severity	
0	Absent: Not detectable on close inspection
1	Present: Clearly present on close visual inspection, not visible to the casual observer, extent not measurable
2	Mild: Limited to the base of the skull, does not extend to the lateral margins of the neck (usually 3 inches in breadth)
3	Moderate: Extending to the lateral margins of the neck (posterior border of the sternocleidomastoid) (usually 3–6 inches) should not be visible when the participant is viewed from the front
4	Severe: Extending anteriorly (6 inches), visible when the participant is viewed from the front
Axilla	
0	Absent: Not detectable on close inspection
1	Present: Clearly present on close visual inspection, not visible to the casual observer, extent not measurable
2	Mild: Localized to the central portion of the axilla, may have gone unnoticed by the participant
3	Moderate: Involving the entire axillary fossa, but not visible when the arm is against the participant's side
4	Severe: Visible from the front or back in the unclothed participant when the arm is against the participant's side
Neck texture	
0	Smooth to touch: No differentiation from normal skin to palpation
1	Rough to touch: Clearly differentiated from normal skin
2	Coarseness can be observed visually, with portions of the skin clearly raised above other areas
3	Extremely coarse: "Hills and valleys" observable on visual examination
Knuckles	Present
	Absent
Elbows	Present
	Absent
Knees	Present
	Absent

normoglycemic Indian cohort was derived as 2.7–17 IU/mL, and 17 IU/mL is proposed as the cutoff for diagnosing hyperinsulinemia in healthy Indians.

Recommendation 2: AN is a cutaneous marker of IR and related conditions such as prediabetes, DM, PCOS, and MS. Its presence should raise an index of suspicion for further investigations.[23]

Obesity, diabetes, hypertension, low physical activity, and a family history of DM and/or hypertension are known risk factors for AN. As weight and body mass index (BMI) increase, the prevalence of AN increases.[24,25] Progression of untreated IR leads to type 2 DM, nonalcoholic fatty liver disease (NAFLD), and MS. A variety of dermatologic manifestations have been linked with DM, AN being one of them. Such skin changes offer insight into patients' glycemic control and could be the first sign of metabolic disturbances in undiagnosed patients.[26,27] Reportedly, 30% of type 1, and 70% of type 2 DM have skin manifestations.[28,29] Prediabetes is a reversible condition; early detection is extremely crucial to prevent further progression.[29,30]

Acanthosis Nigricans and Other Endocrine Disorders

Polycystic ovary syndrome is often associated with AN. Obesity, IR, and hyperandrogenism are seen in patients with PCOS.[31] PCOS patients with a family history of DM and obesity, with a BMI of >30 kg/m^2 and a waist circumference of ≥90 cm are more likely to develop AN, as reported in an Indian study.[32] Hirsutism and AN are the most reliable cutaneous markers of PCOS and warrant further evaluation for metabolic comorbidities.[32,33] Patients with rare conditions such as Cushing syndrome and acromegaly can present with AN.[34,35]

Drug-induced Acanthosis Nigricans

Drug-induced AN is associated with certain medications, and the condition reverses once the medication is stopped. A systematic review has identified 13 drugs responsible for drug-induced AN, of which nicotinic acid was the most common (refer Table 1).[36]

Recommendation 3: All possible causes responsible for AN must be considered to provide appropriate treatment. For suspected drug-induced AN, before stopping the causative medication, a risk–benefit analysis and an available alternative must be evaluated.

Acanthosis Nigricans and Malignancy

Generalized involvement, sudden and rapid onset, location in atypical sites such as palms or mucous membranes, intense pruritus, or thickened velvety palmar folds (tripe palms) are highly suggestive of internal malignancy. Paraneoplastic AN is usually associated with adenocarcinomas of abdominal organs and genitourinary cancers. Regression of AN lesions occurs with the treatment of the underlying tumor, and recurrence of the lesions may precede relapse of the malignancy.

Recommendation 4: The clinician must be aware of the red flags in the presentation of AN suggesting underlying malignancy.

Evaluation of Acanthosis Nigricans and Its Associations

Depending upon the findings of clinical evaluation (Flowchart 1), blood tests, imaging, and other tests may be required to rule out underlying IR, DM, PCOS, MS, or even malignancy. The age of the patient, weight, and family history decide the type of investigations needed (Refer to Tables 6 and 7). The mental status examination may also be considered as required.

Although AN is a reliable cutaneous marker of IR in children as well as adults, documentation of IR can be done by estimating fasting insulin levels only if required; else, it is not recommended. Overweight/obese female adolescents with AN, clinical signs of hyperandrogenism, and irregular menses require work-up for PCOS.

Recommendation 5: To undertake a detailed medical evaluation, including family history and relevant investigations, to rule out the underlying/associated conditions.

Management of Acanthosis Nigricans

Treating underlying/associated conditions and recommending lifestyle changes is the cornerstone of management.

Skin lesions are treated using topical, systemic, and procedural modalities. Complete resolution is difficult to achieve.[12] Psychological stress is very common, hence, counseling should be part of the therapy. A multidisciplinary approach (Flowchart 2) is required for better clinical outcomes.[42] Table 8 briefly describes currently available topical, systemic, and procedural therapies.[43]

Lifestyle Modification

General health factors such as diet control with appropriate nutrition, increased physical activity, normalizing sleep patterns, and reducing stress levels improve metabolic health and help in the resolution of AN. Weight reduction is the most scientific and practical management strategy in the treatment of AN.[12]

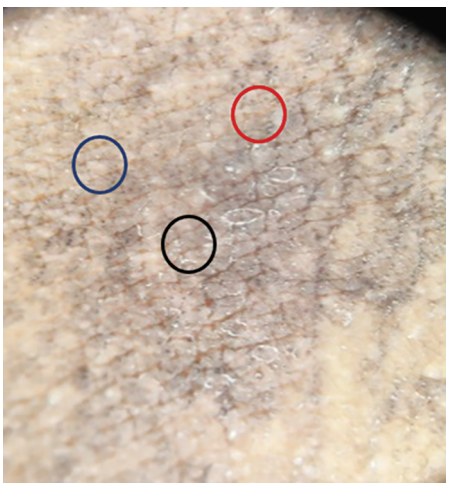


Fig. 2: Dermoscopy of AN (10× magnification); red circle—furrows; black circle—dark structureless areas; blue circle—hyperpigmented areas; Courtesy: Department of Dermatology, MGM Institute of Health Sciences, Kamothe, Navi Mumbai

Table 5: Reported prevalence of AN in associated conditions[11,15–22](evidence level 2)

Associated conditions	*Reported prevalence of AN*
Patients with IR	31.3–59.6%
Patients with type 2 DM	35–72%
Women with PCOS	5.2–77.7%
Patients with MS	68.4%
Obese women with MS	60%
PCOS women with MS	70–82%
Patients with type 1 DM and MS	13%
Obese children and adolescents	86%
Obese adults	74%
Obese PCOS women	39.9%
Lean PCOS women	12–50%
Healthy pregnant women	2.9–49.1%
PCOS women with gestational DM	17.5–62%
Pregnant PCOS with preeclampsia or hypertension	77.7%

Diet

Obesity is an important contributor to IR, PCOS, DM, MS, and other endocrinological disorders.[51–53] A diet comprising 60% of energy from carbohydrates, 15% from protein, 25% from fats, and limiting animal products to a single portion a day, has been shown to increase insulin sensitivity, decrease visceral and subcutaneous fat, significantly decrease inflammation and improve leptin levels.[54] Limiting the consumption of processed foods, refined grains, sugars and foods high in sodium, and trans fats would help in weight loss.[55] Table 9 provides general diet recommendations for Indians.[56]

Exercise

Exercise is a crucial lifestyle management tool for weight loss and weight maintenance.[57] It leads to significant fat loss including visceral fat loss.[57] It also improves IR among prediabetes, DM, obese patients, and overweight children and adolescents.[58–61] It improves insulin sensitivity regardless of the type of exercise program[62] and prompts the release of endorphins bringing in the feeling of well-being. A strong association between physical activity and AN is well-known and established in many studies globally and in India.[63] Recommended activities include walking, jogging, cycling, swimming, playing an outdoor sport, aerobic exercise, resistance training, high-intensity interval training (HIIT), etc.

However, currently, there are no published guidelines that recommend specific exercise regimes to treat AN. In any case, the exercise regime requires customization based on the patient profile, general fitness, accompanying comorbidities, and current fitness literacy. As a general guideline, we can consider a combination of exercises from the American College of Sports Medicine (ACSM) recommendations (Table 10). Increasing physical activity throughout the day by minimizing sedentary time is essential.

Sleep

Poor sleep is known to increase IR and elevates DM risk through multiple pathways. Distortion of metabolic pathways alters glucose metabolism resulting in IR, obesity as well as DM.[64] Poor sleep results in mood swings, irritability as well as elevated blood pressure.[65] Short sleep duration (≤ 6 hours) is known to increase weight ≥5 kg whereas a sleep duration of 9 hours is associated with a reduced risk of weight gain.[66]

Recommendation 6: It is important to advise patients about healthy eating practices, a nutritionally diverse and balanced diet, physical activity, and good sleep habits.

Mental and Psychological Health

Low self-esteem scores have been reported in adolescent obese girls with AN, especially with high insulin and testosterone levels.[67] These may lead to social anxiety and depression. Family involvement is the key to success, especially when AN and IR occur at an early age. Behavioral approaches in terms of diet changes, sleeping habits, engaging in physical activities, and reducing stress yield positive outcomes. Yoga, meditation, and mindfulness practices help toward mental and psychological well-being. Medication for depression may be necessary. Counseling

Table 6: Acanthosis nigricans—basic approach to evaluation

A	History • Onset and progression of AN • Associated symptoms • Medication history • Family history
B	Complete physical examination • Measurement of BMI (normal range for Indians 18.5–22.9 WHO criteria)[37] • Waist circumference: Indian cut-off male >90 cm; Indian cut-off female >80 cm • Waist-to-hip ratio; men ≥0.89; women ≥0.81[38] • Abdominal examination (fatty liver and tumor) • Blood pressure (BP) Evaluation for the presence of hyperandrogenism (hirsutism, acne, female pattern hair loss), genetic disorders, etc.
C	Clinical examination • Morphology of AN for typical skin lesions, location, and distribution

Flowchart 1: Acanthosis nigricans—approach to clinical evaluation

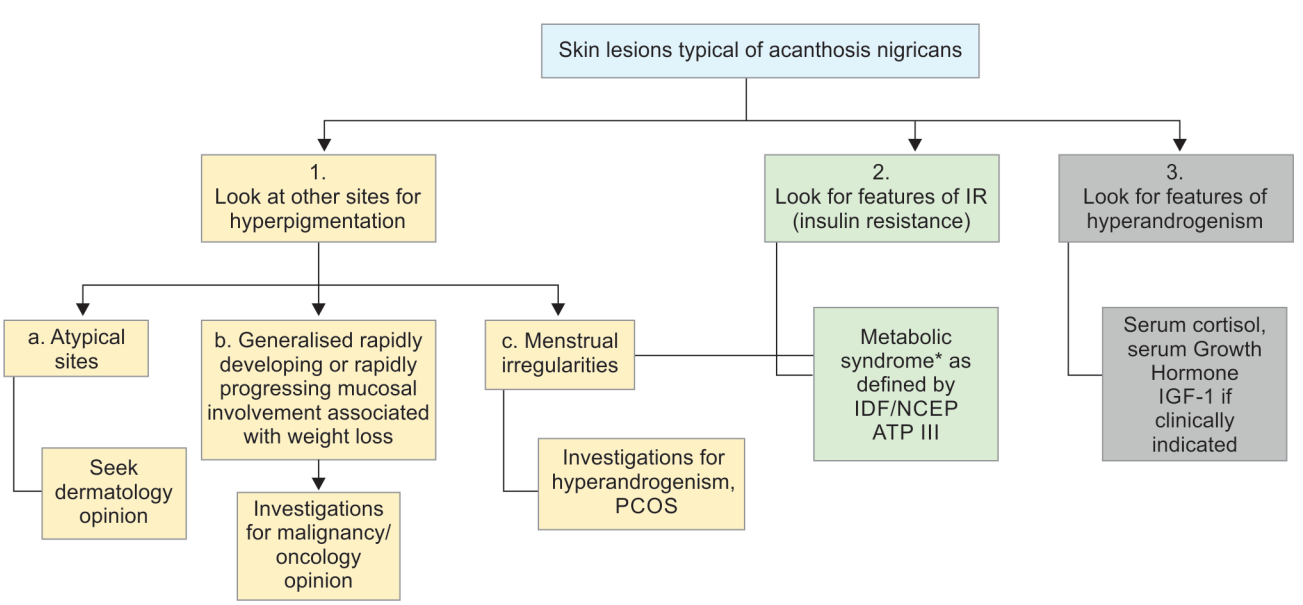


Table 7: Acanthosis nigricans—recommended investigations for associations

Association	*Investigations*
IR	• Fasting insulin level to confirm or exclude IR (insulin value inappropriately high for glucose level)* • Glucose/insulin ratio (<4.5 denotes IR)[39] (level 2) • Homeostasis model assessment-IR (HOMA-IR) (research tool)
Prediabetes	• Fasting glucose: ≥100 mg/dL but <126 mg/dL • Hemoglobin A1c: 5.7 to <6.5% • 2 hours oral glucose tolerance test (OGTT) with 75 gm sugar ≥140 mg/dL and ≤199 mg/dL Should follow ADA recommendations[40] (level 1)
Diabetes	Diagnosis of diabetes is established if any of the following criteria is present and verified on repeat testing as per ADA guidelines[40] (level 1) • HbA1C ≥6.5% • Fasting glucose ≥126 mg/dL • Random plasma glucose ≥200 mg/dL with classic symptoms of hyperglycemia or hyperglycemic crisis
PCOS	• OGTT (as per ADA guidelines)[40] (level 1) • TSH • Prolactin • Total/free testosterone (days 2–5 of menstrual cycle) • 17-hydroxyprogesterone • DHEAS • USG pelvis and abdomen
Lipid abnormality	Classification of results from lipoprotein profile (mg/dL)[41] (NCEP criteria) LDL cholesterol (primary target of therapy) • Optimal: <100 • Near-optimal: 100–129 • Borderline high: 130–159 • High: 160–189 • Very high: ≥190 Total cholesterol • Desirable: <200 • Borderline high: 200–239 • High: ≥240 HDL cholesterol • Low: <40 (risk factor) • High: ≥60 (desirable) Triglycerides • Normal: <150 • Borderline high: 150–199 • High: 200–499 • Very high: ≥500
Liver enzymes (transaminase levels)	To look for NAFLD
Thyroid abnormalities	Thyroid profile: TSH
Sudden onset of AN or rapidly progressive AN	Evaluation for underlying malignancy • Complete blood count • Stool test for occult blood • Chest and abdominal X-ray/CT/MRI • Abdominal and pelvic ultrasonography • Gastrointestinal endoscopy

*, Generally, not recommended; at the discretion of the treating clinician and/or for research purposes

Flowchart 2: Management of AN and associated conditions

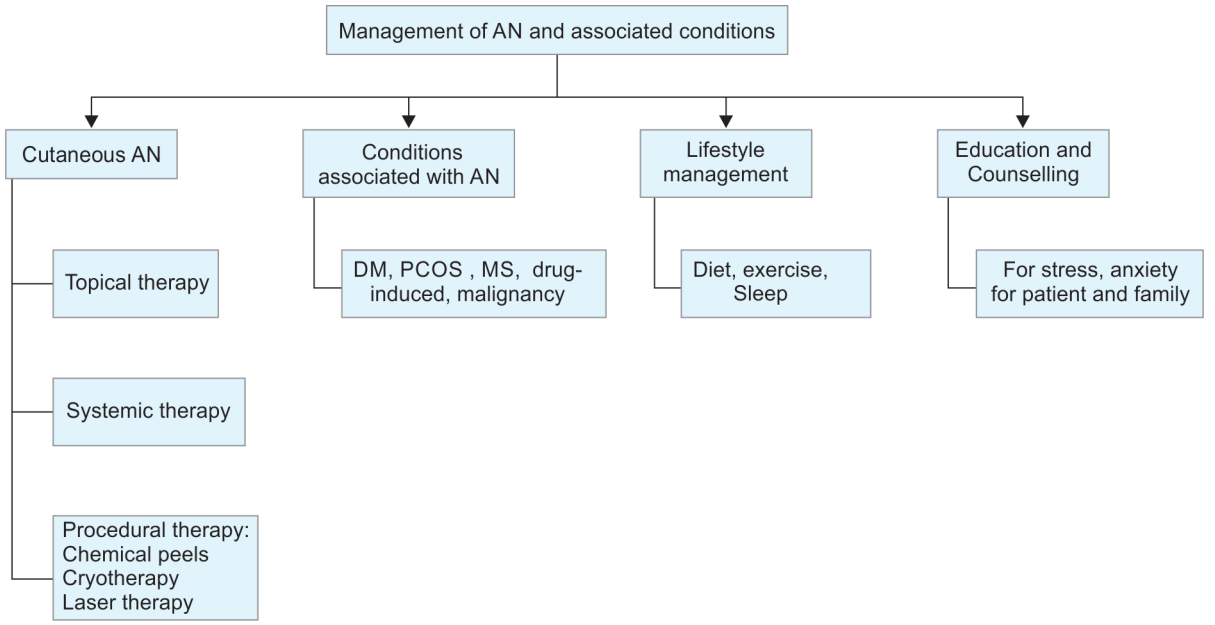


Table 8: Acanthosis nigricans—treatment modalities

Classification	*Therapy*	*Details in brief*	*Reference number and level of evidence*
Topical therapy			
Retinoids	Tretinoin, (0.025, 0.05%) and adapalene (0.1%)	• Alters epidermal turnover and epidermal keratinization • Treatment duration 4–14 weeks • Risk of relapse on stopping treatment	44; level 2
Topical vitamin D analogs	Calcipotriol (0.005%)	• Inhibits keratinocyte proliferation • Promotes differentiation by increasing keratinocyte intracellular calcium and cyclic GMP levels. Treatment duration 3 months	42; level 2
Other topical treatment	Urea (10 and 20%), glycolic acid (GA) (20–70%), lactic acid (ammonium lactate 12%) and salicylic acid–mandelic acid chemical peel combinations; TCA peel (15 and 20%)	• Acts by keratinolysis • Safe and effective	42; level 2 45; level 3
Systemic therapy			
Oral Hypoglycemic agents*	Metformin (dosage range 500–1500 mg per day)	• Improves insulin sensitivity • Reduces hyperinsulinemia, body weight, fat mass • Can be combined with other OHAs/insulin	2; Level 2 1; level 2 46; level 1 47; level 5
Antioxidants	α-lipoic acid (ALA) (400 mg per day)	• Potent biological antioxidant • Enhances insulin sensitivity, improves the signs of AN	48; level 1
Oral retinoids	Isotretinoin, acitretin (3 mg/kg/day)	• Acts by normalizing epithelial growth and differentiation. • Not recommended for young women with AN due to teratogenic effects • Duration: 2 months	1; level 2 42; level 2
Procedural treatment			
Chemical peels	Trichloroacetic acid (TCA) peels 15%	• Acts by precipitation of proteins in epidermal cells • Causes necrosis and destruction of the epidermis leading to reepithelialization • Safe, easy accessibility, inexpensive	49; level 2 42; level 2
Cryotherapy	Liquid nitrogen/cryogen	• Acts by tissue damage due to freezing • Efficacy depends on depth and extent of lesions, duration and number of freezing cycles	43; level 4
Laser therapy	Alexandrite, fractional CO_2 550-nm erbium fiber laser	• Destroys AN lesion without damaging the surrounding tissues • Available laser treatment protocols • Alexandrite—every 3 weeks for five sessions • Fractional CO_2—every 4–6 weeks for maximum four sessions • 550-nm erbium fiber—every 4 weeks for maximum three sessions	50; level 1

*, Beneficial effects of sitagliptin and pioglitazone in treatment of AN are reported[42]

of the patient and family can be done by the clinician or by seeking professional help from a psychologist or psychiatrist. Please refer to Flowchart 3 for recommended steps for the prevention and management of AN in children.

Table 11 provides the summary of all recommendations suggested in this manuscript.

Recommendation 7: Physical and mental well-being should receive equal emphasis. Education and counseling are crucial for initiating and sustaining lifestyle changes.

Table 9: Steps toward a healthy and nutritious diet: dos and donts

Do's

- Diverse food plate with different food Groups (NIN, ICMR, My Plate for the day 2020. https://www.nin.res.in/)
- Daily diet to include plant proteins (pulses, dals, peas, beans, nuts, and oilseeds)
- Cereal pulse combination (roti usal or dal; dal chawal) along with curd or milk
- Include a diet with high omega 3 and MUFA (black chana, cow pea (chawli), urad dal, rajmah, soyabean, nuts, seeds, cereals green leafy vegetables)
- Limit the quantity of cooking oil (approximately 500 gm/adult/month); use of MUFA rich oil (rice bran, til, groundnut), omega 3 rich oil (soyabean, mustard), or a blended oil
- Use prebiotic foods high in dietary fiber and resistant starch (raw banana, chick pea, whole moong, bajra flour, etc). Enhance the prebiotic effect by soaking, steaming, cooling, and roasting with limited oil
- Regularly consume probiotic food items such as curds, etc.

Dont's

- Avoid salt intake above one level teaspoon (5 gm) per day.
- Minimize added sugars in foods and beverages
- Avoid refined flour, saturated fats, and trans fats foods like khari, pav, maida roti, doughnuts, pastries, cakes, biscuits, etc.
- Minimize the use of packaged and processed food

Table 10: Exercise recommendations for AN (adapted from the ACSM's guidelines for exercise prescription for overweight and diabetes conditions)

	Aerobic	*Resistance*	*Flexibility*
Frequency	>3 days/week	2–3 days/week. Nonconsecutive days	>2–3 days/week
Intensity	Moderate (40–59% of HRR or VO_2R) to vigorous (>60% HRR or VO_2R) intensity as per fitness levels. May have to start with low intensity initially but goal should be to progress	Moderate (50–69% of 1RM) to vigorous (70–85% of 1RM)	Stretch to the point of tightness or slight discomfort
Time	30 minutes/day (150 minutes/week) progressing to 60 minutes/day (250–300 minutes/week)	2–4 sets of 8–12 repetitions of 8–10 exercises involving major muscle groups	Static stretches for major muscle groups to be held up to 30 seconds and to be done 2–4 times
Type	Prolonged, rhythmic activities using large muscle groups (e.g., walking, jogging, cycling, swimming)	Resistance machines, free weights, resistance bands or body weight	Combination of static and dynamic

1RM, 1 repetition maximum; HRR, heart rate reserve; VO_2R, VO_2 reserve (maximal oxygen uptake); intensity of exercise is calculated using the following methods—HRR method: target HR = $[(HR_{max} - HR_{rest}) \times \%$ intensity desired$] + HR_{rest}$; VO_2R method: target $VO_2R = [(VO_{2max} - VO_{2rest}) \times \%$ intensity desired $+ VO_{2rest}$; 1RM: the maximum weight that can be lifted for a single repetition

Flowchart 3: Approach to AN in pediatric age-group

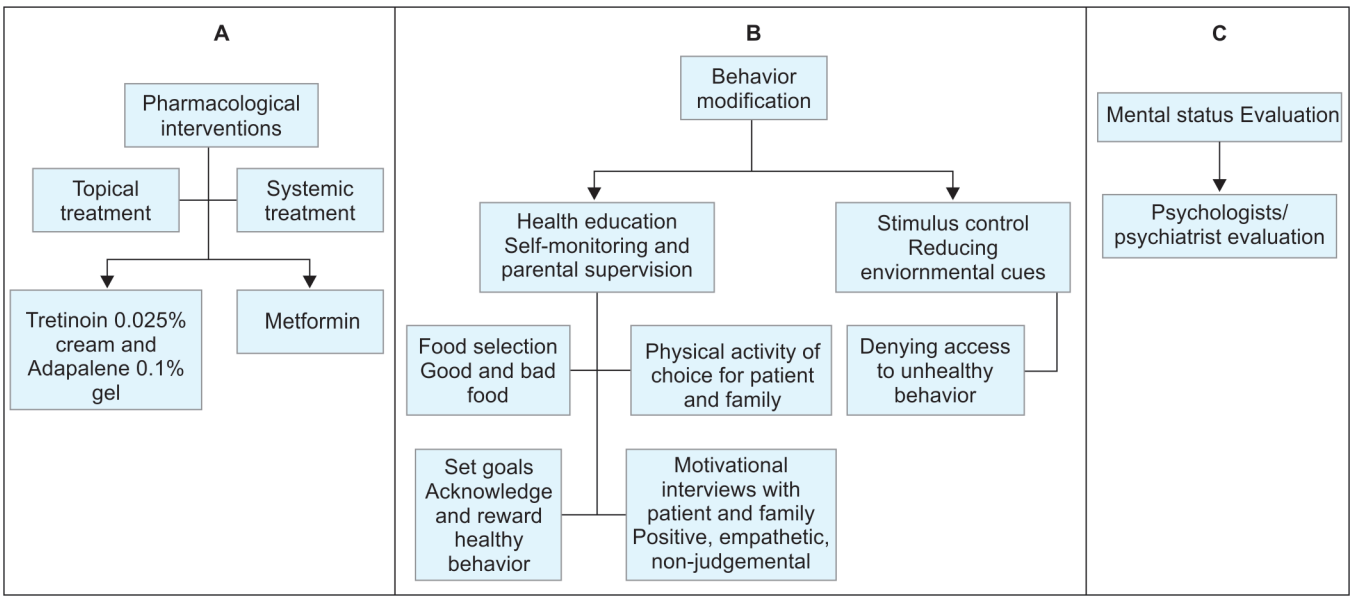


Table 11: Summary table of recommendations

Recommendations	*Expected outcomes*
Recommendation 1: AN can be suspected from general skin examination due to its classical clinical appearance on typical sites	Early detection of IR cases
Recommendation 2: AN is a cutaneous marker of IR and related conditions such as prediabetes, DM, PCOS, and MS. Its presence should raise an index of suspicion for further investigations	An appropriate investigational plan can help detect the root cause of AN
Recommendation 3: All possible causes responsible for AN must be considered to provide appropriate treatment. For suspected drug-induced AN, before stopping the causative medication, risk–benefit analysis and an available alternative must be evaluated	Clinicians can be made aware of drug-induced AN and can advise the patient accordingly
Recommendation 4: The clinician must be aware of the red flags in the presentation of AN suggesting underlying malignancy	Atypical AN due to underlying malignancy can be detected early for better prognosis
Recommendation 5: To undertake a detailed medical evaluation, including, family history, and relevant investigations to rule out the underlying/associated conditions	Early diagnosis helps in timely management and reducing morbidity
Recommendation 6: It is important to advise patients about healthy eating practices, a nutritionally diverse and balanced diet, physical activity, and good sleep habits	Lifestyle changes shall help attain good metabolic health
Recommendation 7: Physical and mental well-being should receive equal emphasis. Education and counselling are crucial for initiating and sustaining lifestyle changes	Motivation and self-esteem improve emotional health and contribute to good quality of life
Recommendation 8: It would be appropriate and timely to integrate AN as a simple, visible, screening sign for early detection of IR in National Health Programmes	Allows diagnosis of previously undetected or missed cases of prediabetes, DM, and MS in the community

Challenges and Call for Action

The Government of India, recognizing the need to control the rise of NCDs, proactively launched the National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases, and Stroke (NPCDCS) in 2010. The main focus of this program is health promotion, early diagnosis, management, and referrals for positive health outcomes. The NCD program currently focuses only on adults aged 30 years and above. They have a well-defined risk score to identify NCD cases for referral. AN would be a highly useful addition to the risk score.

The National Diabetes Control Programme focuses on the early detection and management of prediabetes and DM. However, India still has 69.2 million people with DM and 36.5 million with prediabetes. The Indian Council of Medical Research-India Diabetes (ICMR-INDIAB) study, conducted in all 30 states/union territories of India between 2008 and 2020, has reported a 150% increase in DM cases, with the young population between the ages of 25–34 years being affected. Unfortunately, every sixth diabetic person in the world is Indian.[68]

The Ministry of Health and Family Welfare has also launched a health program for adolescents (age-group of 10–19 years), namely Rashtriya Kishor Swasthya Karyakram (RKSK), which addresses issues such as nutrition, reproductive health, NCDs, mental health, and substance abuse.

India has a huge experience with its trained workforce to reach the local population at the remotest of places through National Health Mission programs. Grassroots healthcare workers, namely auxiliary nurse midwife (ANM), accredited social health activist (ASHA), anganwadi worker (AWW), who are directly in contact with Indian households in every urban and rural area could be trained to detect AN and report to the primary healthcare center (PHC). The PHC can then undertake certain tests and provide counseling for lifestyle changes and further management. School health programs could incorporate this sign as one of the components of school health checkups. Adequate linkage to NCD program needs to be ensured such that the child is followed up to assess further risks.

It is reported that approximately 57% of individuals continue to remain undiagnosed for diabetes in India.[69] The inclusion of AN in National Health Programmes can help to detect these currently missed cases.

Recommendation 8: It would be appropriate and timely to integrate AN as a simple, visible, screening sign for early detection of IR in National Health Programmes.

Conclusion

Acanthosis nigricans is a reliable and easy-to-detect marker of IR. It should be an integral part of the routine general examination by clinicians and healthcare workers (HCWs). India has a huge burden of NCDs such as DM, MS, and PCOS. Hence, early detection of IR and its appropriate management is crucial. AN must receive its due attention and incorporation into the national health mission programs. Training modules for the detection of AN need to be disseminated to all clinicians and healthcare workers.

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