ACANTHOSIS NIGRICANS:
A RISK FACTOR FOR TYPE II DIABETES

By

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Abstract:
This paper serves as a review of Type II diabetes and pre-diabetes and their associated risk factors: obesity, race, age, and family history of the disease. A new risk factor, Acanthosis Nigricans, is examined in ordinance with common diabetes risk factors, and correlations are drawn between its occurrence and Type II diabetes. Acanthosis Nigricans is a skin condition that can be non-invasively identified. With the current rise of diabetes and obesity in children and adults, finding an easily identifiable risk factor is pertinent for catching the disease in the pre-diabetic state before Type II diabetes is developed. The role of Community Health Workers in disease prevention and intervention was also examined.
In our findings, Acanthosis Nigricans is indicative specifically of development of insulin resistance and is most often seen in Hispanic and Black populations. Decreases in physical activity and increases in food-insecure households puts children at higher risk of diabetes development than ever before. Community Health Workers serve as a critical link between families in low-income communities and adequate health education. With proper training, community health workers have the potential to help low-income families stop the development of Type II diabetes in their children before it begins.
As researchers focus on finding cures for cancer and Alzheimer's disease, and as the public participates in ALS ice bucket challenges on social media, many people often overlook an ever-increasing epidemic that is taking over the country: Diabetes is one of the most prevalent diseases in the United States today and the 7th leading cause of death in the U.S. Annual costs exceed $245 billion in treatment and loss of productivity due to illness. Approximately 9% of the U.S. adult population has diagnosed diabetes as well as around 208,000 (.25%) children under the age of 20. However, alarmingly, 27% (or 86 million) are estimated to have prediabetes, an intermediate disease state that serves as a precursor to Type II diabetes. A majority of prediabetics remain unaware of their condition or that they are at risk.

There are two types of diabetes: Type I diabetes is a condition in which insulin producing cells (pancreatic beta cells) either do not function properly or are destroyed by one's own immune system. Insulin is a hormone produced by the pancreas, and is the key regulator of blood sugar homeostasis. Normally, insulin binds its cell receptor, causing translocation of glucose transporters to the plasma membrane, allowing glucose to enter the cell to be used for energy, thereby lowering blood sugar levels to normal. Without insulin, the body cannot regulate glucose levels; chronic high blood glucose can damage arterial walls, which contributes to atherosclerosis and neuropathy among other conditions.

Type II diabetes is a disease that develops slowly over decades, and is highly associated with excess body weight. Unlike Type 1 diabetes, Type II diabetes is characterized by insulin resistance rather than an absence of insulin. There is an intermediate stage before development of Type II diabetes, however, called pre-
diabetes. Pre-diabetes is characterized by intermediate read-outs on typical tests for diabetes. A value between 5.7% and 6.4% for the glycated hemoglobin test is considered pre-diabetic, whereas anything above 6.4% is considered definitive of diabetes. Fasting blood glucose levels between 100 and 125 mg/dL are pre-diabetic, and, similarly, anything above 125 mg/dL is considered as Type II diabetes. Pre-diabetes is different from Type II diabetes because the body is still relatively sensitive to insulin. Type II diabetes begins when a person has pre-diabetes and maintains a chronically high carbohydrate, sugar, and fat diet rather than taking measures to adjust their lifestyle. These factors constantly signal for the pancreas to produce insulin, which, over time, causes the beta cells to become less sensitive to changes in blood sugar. In this case, the body is still producing insulin, but not at sufficient levels to adequately lower blood sugar. Both prediabetes and Type II diabetes are reversible with changes in diet and exercise habits and weight loss. However, if the condition persists, beta cells will begin to degrade and apoptose, leading to insulin dependence. As Type II diabetes becomes more prevalent, especially in children, it is crucial to discover and develop screening tools for community based health centers to use to identify risk factors and inform families of their potential risks for developing the disease so that the appropriate prevention strategies can be initiated.

Increased diabetes prevalence in children and adults is associated with several factors: the number of households nationwide reporting as “food-insecure”, decreased physical activity and increased sedentary behavior, and an increase in development of gestational diabetes and weight gain before and during pregnancy. These factors contribute to the development of obesity, the major risk factor for diabetes. In 2014,
38% of U.S. adults were obese. This increase in obesity and related diseases cost the nation over $210 billion in healthcare spending that is considered preventable\(^7\). The most startling factor in this epidemic is the rise in childhood obesity. Although recent census results show a leveling-off of the obesity rate, in 2014, 17.2% of children aged 2-19 were classified as obese up from around 10% in 1988\(^7,8\). In Hispanic and Black populations, there is a higher level of obesity seen in both children and adults compared to White populations\(^8-12\). Several states located in the deep south (AL, AR, GA, LA, MS, TN) have the highest concentrated rates of obesity and hypertension reported\(^1,13\), and this trend carries over into diabetes incidence as well as the highest rates of diabetes are also seen in the same area\(^1\). Managing sedentary activity level and eating habits and overcoming income inequality factors will play a critical role in lowering the incidence of diabetes nationally.

Type II diabetes, if diagnosed early, is reversible; the key is identifying those at risk and ensuring that they are educated about their risk. The major risk factors are obesity, family history of Type II diabetes, Hispanic, American Indian or Black ethnicity, and level of sedentary activity. Pre-diabetes prevalence in children is not well studied, but studies that have been conducted show certain levels of prediabetes in children. One study of 3383 children age 12-19 randomly selected from an NHANES census report found pre-diabetes prevalence of 23% in 2008, which is up from 9% in 1999\(^14\). It is crucial to understand and recognize risk factors to prevent these children from developing Type II diabetes.

One risk factor for diabetes that has recently come to attention is called Acanthosis Nigricans (AN). AN is a dermatological condition highly associated with
insulin resistance. There are several types of AN. Type 3 AN, specifically, is associated with diabetes development and manifests as velvet-textured patches of darkened skin. These patches occur in skinfolds: most commonly on the neck, armpits and elbows, and often near the groin, knees, and folds of skin present on the stomach\textsuperscript{15}. AN is thought to arise due to high levels of keratinocyte and fibroblast proliferation, though why higher concentrations are only found in areas of the skin is not well understood\textsuperscript{15}. Descriptive scales have been developed for AN recognition, rating the severity of skin texture and color, as well as the presence of darkened skin on the knuckles, elbows and knees\textsuperscript{16}. Further development of these scales will allow clinicians to determine disease risk based on AN severity. In order to elucidate the incidence of AN, studies have been and are currently being conducted to identify whether there are associations between AN and Type 2 diabetes risk factors. In one study of 1133 patients from various ethnic backgrounds, ages 7-39, several diabetes risk factors were examined: BMI, hypertension, dyslipidemia, age, family history, physical activity levels, and ethnic background\textsuperscript{12}. Patients were screened for these factors along with presence of AN. The study concluded that as the number of risk factors increases, so does the prevalence of AN. AN was found in 17\% of children and 21\% of adults, and patients with AN were almost twice as likely to have Type II diabetes than those without. The study also showed that Hispanics, Blacks, and American Indians had a higher prevalence of Type II diabetes than Whites\textsuperscript{12}. Although the paper does not make any conclusions about higher prevalence of AN in ethnic backgrounds, the higher incidence of Type II diabetes in these populations suggests increased rates of AN. In another study, a sample of 1,412 randomly chosen children from a school in Texas were screened for presence of
AN. A specific finding from this study was that ethnicity is associated with AN prevalence. 5.5% of Hispanic and 13.3% of Black children were found with AN compared to less than 0.5% of White children in the study\textsuperscript{17}. These children were also screened for fasting plasma insulin, showing that higher fasting plasma insulin levels correlated with presence of AN as well\textsuperscript{17}.

As prevalence of diabetes in children continues to increase, AN is becoming increasingly relevant for early diagnosis and prevention of Type II diabetes. AN in children initially presents itself on the folds of the neck, and is often mistaken for dirty skin\textsuperscript{18}. Although studies tend to interpret AN as correlating strongly with obesity, a study in children ages 8-14 demonstrated that AN can be used as an indicator of insulin resistance in children, but cannot necessarily be used as an indicator for other metabolic risk factors such as dyslipidemia\textsuperscript{19}. In this study, all children studied were clinically obese, but only 236 children had AN and 51 children did not. Several screens were performed and information gathered to determine why some obese children did not develop the condition, including measuring fasting glucose and insulin levels, triglycerides, and HDL levels. The most significant difference was that the obese children with AN showed signs of insulin resistance and abnormal glucose homeostasis compared to obese children without AN\textsuperscript{19}. Correlations between AN and dyslipidemia and cholesterol were relatively insignificant. With a better understanding of what AN can indicate about a patient, clinicians and health workers will be able to guide patients to a proper prevention or treatment plan.

One ever-increasing issue relating to diabetes diagnosis is accessibility to healthcare. AN is most prevalent in Hispanic, American Indian, and Black populations,
often due to poor living conditions and low-income. Increased rates of hypertension\textsuperscript{13}, diabetes\textsuperscript{1}, and obesity\textsuperscript{7} as well as decreased physical inactivity\textsuperscript{5} all show a correlation of occurrence. These factors coincide with national poverty levels, as we see increased incidence of poverty\textsuperscript{20} by state and overall. Low-income families cannot afford to buy adequate food, and much less can they afford adequate healthcare. This has created a disadvantage for these families, as they are the ones in most need of healthcare and life-style and nutritional education. Even if physicians are able to recognize AN, they will seldom come in contact with those who need the diagnosis. So, what is the best method to inform these families about their risks and their life-style choices?

Community Health Centers (CHCs) were developed to help the poor receive the healthcare they need. Although the quality of care is not always paralleled to that seen in a physician’s office, CHCs are the first step toward equal healthcare, and adequate training of community health workers can help identify people at risk for Type II diabetes development. Disadvantaged families are primarily found at CHCs for their health concerns, and the incidence of chronic disease (diabetes, asthma, hypertension, etc.) in families attending CHCs is 50% higher than families attending physician’s offices\textsuperscript{21}. This provides an opportunity for the Community Health Workers (CHWs) to recognize AN as a precursor to Type II diabetes. In one of the studies previously mentioned, when patients discovered they had AN, it prompted more discussion about lifestyle changes than if they only had conditions such as insulin resistance or dyslipidemia\textsuperscript{12}. Several clinicians in the study noted the change in patient behavior when diagnosed with AN, finding that the patients became more inclined to inquire about treatment options and lifestyle changes than normal. This implies that CHWs using AN as an identification
factor can potentially influence how the patient responds to their diagnosis and how willingly they will be to seek treatment. In order to elucidate the impact of CHWs on disease diagnosis, the Health Resources and Services Administration conducted 44 interventions at various CHCs. These interventions included teaching CHWs about the most effective ways to treat chronic diseases, about how to improve the quality of care given to their patients, and letting CHWs share their own experiences and teach one another in the facility. The 44 intervention centers were then compared to 20 centers than had not been included in the intervention scenario. Their results showed increased screening tools utilized for early diabetes diagnosis as well as increased diagnosed and treatment for asthma patients in the intervention centers compared to those not intervened\textsuperscript{22}. These findings demonstrate that Community Health Centers can readily improve their quality of care and diagnoses potential by having staff meetings and teaching their employees about the current standards of care. CHWs are also important because they are usually from the communities in which they work. They can relate to their patients on a level that most physicians cannot, which develops a more open relationship with patients. CHWs are able to reach a subset of the population that standard clinicians cannot, and are often the only source of health and wellness information these populations will receive\textsuperscript{23}. As AN becomes a more prominent tool for identifying insulin resistance, it will be pertinent for CHCs to teach this information to their employees to help recognize pre-diabetes before it manifests into Type II diabetes.

Not only CHWs play a role in pre-diabetes diagnosis, however. Every day children encounter all sorts of caregivers, including teachers, school nurses, nannies and daycare employees. These individuals have the potential to recognize AN in children,
and they all can contribute to early recognition. Most of these people are not aware of AN as a risk factor for diabetes, though. Development of AN screening tools that can be printed out and hung up in nurse’s offices or that can be included in Community Health Center pamphlets for families to take home will be a first step in making this information accessible to the public. However, most people are visual learners, which poses a problem: Hispanic children will have AN that appears different than Black children due to initial skin color. Visual AN screening scales could potentially be developed according to ethnic background or original skin color, but for now descriptive scales are the common diagnostic tool.

As AN screening becomes more well-known and commonly practiced, it should slowly be integrated as a standard of care for obese children and families to facilitate early insulin resistance recognition. Early identification should be followed by a relative decline in development of Type II diabetes seen in children, carrying over into lower prevalence seen in adults. With recent changes in the economy, like increases in minimum wage, affordable healthcare, and movements for improvements in public education, some low-income families will hopefully see an improvement in their quality of living. This means being able to afford quality food for their families and receiving proper prenatal care and learning about the importance of their children’s nutrition. Programs implemented in Community Health Centers and public schools that help educate families about their diet and exercise habits are the first line of defense against obesity and pre-diabetes development. Being able to recognize AN in these communities will serve as another important factor in preventing children from
developing long-term health problems by catching pre-diabetes before it turns into Type II diabetes.

Given the sensitive nature of health status, especially in children, it is important to consider the following when designing a training program for CHWs or other community workers. The first part of training would include teaching CHWs how to recognize the condition. Recognition requires knowledge of populations at increased risk of insulin resistance and diabetes. However, recognition is only the first step. CHWs need to be able to effectively explain AN to families. This means CHWs must know about the relationship of AN with other risk factors for diabetes. Another potential obstacle is informing parents that their child is at risk of developing a serious disease: parents may not be open to the idea that their child has health problems to which they might be contributing. Thus, it is important that CHWs do not relay information in an accusatory fashion. Instead, presentation of the facts about risk factors and development of diabetes will be more effective. It’s also important to let families know right away that these conditions are reversible with lifestyle changes. After recognizing and explaining AN and diabetes, CHWs should not be giving diagnoses, but rather they should be referring patients to see qualified professionals about their conditions. In cases of families that cannot afford to see a physician, CHWs should make some lifestyle modification suggestions and refer families to a nearby Federally Qualified Health Center for further evaluation. It’s important for CHWs to not cross over into diagnosis of disease, because they are not qualified to do so. Their role is to relay information to patients that they otherwise would not have received.
Type II diabetes is becoming increasingly prevalent across the country as rates of obesity and poverty increase. Educating the public about their risk for disease development is pertinent to reverse this trend. One of the most prominent medical fronts that interacts with people who are at the highest risk for diabetes development are CHWs. Therefore, it is important to ensure that information about AN screening tools and other diabetes risk factors are relayed to CHWs, as they are often the first step in disease intervention. Informing families about detrimental lifestyle choices and how they can be affecting their children will help spread awareness and potentially stop diabetes and pre-diabetes development before it starts. If trends continue to increase without medical involvement, the CDC speculates that 1 in 3 North Americans will have Type II diabetes by year 2050\textsuperscript{24}. Changing the course of this trend is feasible only with increased medical intervention, starting at the level of CHWs.
References

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