University of Khartoum
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The prevalence of hyperglycemia among patients with accrochordons (Skin Tags) in Khartoum state

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Dedication

To our great fathers

&

Lovely mothers

To our brothers & sisters

To everyone who encourage us

To all who teach us a letter

Alaa, khalida, Sara & Marwa
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To every person gave us something to light our pathway, we
thank them for believing in us.
## Abbreviations

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<td>AN</td>
<td>Acanthosis nigrican</td>
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<tr>
<td>BMI</td>
<td>Body Mass Index</td>
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<td>DKA</td>
<td>Diabetic Ketoacidosis</td>
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<td>DM</td>
<td>Diabetes Mellitus</td>
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<tr>
<td>FBS</td>
<td>Fasting Blood Sugar</td>
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<td>GL</td>
<td>Glycemic load</td>
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<td>IDDM</td>
<td>Insulin Dependent Diabetes Mellitus</td>
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<tr>
<td>IGF-1</td>
<td>Insulin like Growth Factor-1</td>
</tr>
<tr>
<td>IGFBP-3</td>
<td>Insulin like growth factor binding protein3</td>
</tr>
<tr>
<td>NIDDM</td>
<td>None Insulin Dependent Diabetes Mellitus</td>
</tr>
<tr>
<td>OGTT</td>
<td>Oral Glucose Tolerance Test</td>
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<tr>
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<td>Skin Tags</td>
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Abstract

Background: Skin Tags (acrochordons) are common benign skin tumors that occur in old subjects. There is a possible association between skin tags and impaired carbohydrate metabolism in type II diabetic patients.

Study Design: cross-sectional descriptive study.

Study area: Khartoum state.

Objective: To estimate the prevalence of Diabetes Mellitus among patients with acrochordons (Skin Tags).

Method: Ninety six Sudanese patients with different ages, 53(55.2%) females and 43(44.8%) males with at least three Skin Tags were included. Their fasting blood sugar level was measured.

Results: Among these patients included in this study we found that 44 patients (45.8%) were Diabetic and 21 patients (21.9%) had impaired Fasting Blood Sugar. There was a significant correlation between Fasting Blood sugar level and numbers of Skin Tags ($P = 0.001$). No association was found between skin tags numbers and gender ($p=0.547$); however it significantly correlates with age ($p=0.000$).

Conclusion: There was an association between Skin tags and Diabetes Mellitus.
خلفية الدراسة:
الزوائد الجلدية (النخل) هي ورم جلدي حميد يحدث عند الأشخاص في فترات عمرية كبيرة. ربما تكون هناك علاقة بين هذه الزوائد الجلدية والخلل في استقلاب المواد الكربوهيدراتي عند الأشخاص المصابين بداء السكري من النوع الثاني.

نوع الدراسة: دراسة وصفية مستعرضة.
مكان الدراسة: ولاية الخرطوم.
هدف الدراسة: سنقوم في هذه الدراسة بتحديد انتشار مرض السكري عند الأشخاص المصابين بالزوائد الجلدية.
طرق الدراسة: إشتملت الدراسة على ستة وتسعةون شخصاً في ولاية الخرطوم في فترات عمرية مختلفة. 53 (55.2%) من النساء و43 (44.8%) من الرجال يعانون من ثلاثة زوائد جلدية على الأقل. تم قياس الجلوكوز في الدم لهؤلاء الأشخاص وهم في حالة الصيام.
نتيجة الدراسة: وجدنا أن من بين الأشخاص الذين شملتهم الدراسة هناك 44 شخصاً (45.8%) مصابين بداء السكري و21 شخصاً (21.9%) في مرحلة خلل توازن السكر. والعلاقة المتبادلة ما بين معدل السكر في حالة الصيام وعدد الزوائد الجلدية عند هؤلاء الأشخاص ذو دلالة مع قيمة احتمال (0.001). ليست هناك علاقة ما بين عدد الزوائد الجلدية وجنسي الأشخاص (قيمة الاحتمال 0.547) ولكن هناك علاقة ذو دلالة عالية بينه وبين العمر (قيمة الاحتمال 0.000).
خلاصة الدراسة: هناك علاقة بين الزوائد الجلدية (النخل) وداء السكري.
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Chapter one

Introduction

And

Literature review
1.1. Introduction:

1.1.1. Diabetes Mellitus:

Diabetes Mellitus is a systemic metabolic disorder characterized by tendency to chronic hyperglycemia with disturbances in carbohydrate, fat, and protein metabolism that arises from a defect in insulin secretion or action or both. \(^{(1)}\)

When fully expressed diabetes Mellitus is characterized by fasting hyperglycemia but the disease can also be recognized during less overt stages most usually by the presence of glucose intolerance. \(^{(2)}\)

1.1.1.1. Pathophysiology of diabetes mellitus:

**Physiology:**

Glucose is the primary source of energy in humans. The nervous system, including the brain, totally depends on glucose from the surrounding extracellular fluid (ECF) for energy production. Nervous tissue cannot concentrate or store carbohydrates therefore, it is critical to maintain a steady supply of glucose. \(^{(3)}\)

Dietary carbohydrates are digested in the gastrointestinal tract to simple monosaccharides which are then absorbed. Starch provides glucose directly, while fructose (from dietary sucrose) and galactose (from dietary lactose) are absorbed and also converted into glucose in the liver. \(^{(4)}\)
Control of blood glucose is under two major hormones; insulin and glucagon. (5)

Insulin is a small protein synthesized in beta cells of the islets of langerhans of the pancreas it acts through membrane receptors and its main target tissues are liver, muscles and adipose tissue (4).

It is responsible for the entry of glucose into cells and is the only hormone that decreases glucose level and can be referred to as a hypoglycemic agent. The release of insulin causes an increased movement of glucose into cells and increased glucose metabolism. It is normally released when glucose levels are high and is not released when glucose levels are decreased. It decreases plasma glucose level by increasing the transport entry of glucose in muscle and adipose tissue by way of nonspecific receptors. It also increases glycogenesis, lipogenesis, glycolysis and inhibit glycogenolysis. (5)

The effects of insulin are opposed by other hormones, glucagon, adrenaline, glucocorticoids and growth hormone. (4)

Glucagon is a twenty nine polypeptide hormone secreted by the alpha cells of the pancreatic islets; its secretion is decreased by a rise in the blood glucose concentration. In general its action opposes that of insulin; it stimulates hepatic (not muscle) glycogenolysis through activation of glycogen phosphorylase, gluconeogenesis, lipolysis and ketogenesis. (1)
Epinephrine is produced by the adrenal medulla and it increases plasma glucose by inhibiting insulin secretion, increasing glycogenolysis and promoting lipolysis.\(^5\)

Cortisol is released from the adrenal cortex on stimulation by adrenocorticotropic hormone (ACTH). It increases plasma glucose by decreasing intestinal entry into the cell and increasing gluconeogenesis, liver glycogen and lipolysis.\(^6\)

Growth hormone is released from the anterior pituitary gland and it increases plasma glucose by decreasing the entry of glucose into cells and increasing glycolysis.\(^5\)

Adrenocorticotropic hormone (ACTH) stimulates adrenal cortex to release cortisol and increases plasma glucose levels by converting liver glycogen to glucose and promoting gluconeogenesis.\(^5\)

Thyroxin is the thyroid hormone that increase plasma glucose level by increasing glycogenolysis, gluconeogenesis and intestinal absorption of glucose and is not directly involved in glucose homeostasis.\(^6\)

Somatostatin is a fourteen amino acids peptide found in the gastrointestinal tract and the hypothalamus and it is produced by the beta cells of the islets of langerhans in the pancreas. It increases plasma glucose level by the inhibition of insulin, glucagon growth hormone and other endocrine hormones.\(^5\)(6)
Plasma glucose level is a balance between these different endocrine forces. \(^4\)

**Hyperglycemia:**

When there is a metabolic failure to maintain homeostasis and the rate of glucose production exceeds the rate of consumption, blood glucose concentration rises. As described above, when hyperglycemia happens, diabetes is diagnosed. Glucose production greater than consumption is due to an inappropriate decline in the ratio of insulin to glucagon or decrease in insulin action or combination of both insulinopenia and insulin resistance. \(^7\)

**1.1.1.2. Etiological classification of diabetes mellitus (WHO classification):**

Diabetes Mellitus are classified into Type 1 diabetes, Type 2 diabetes, Other Specific types and Gestational Diabetes. \(^8\)

**Diabetes mellitus type I:**

It is also named type I diabetes, insulin dependent diabetes mellitus, (IDDM). It is a result of cellular-mediated autoimmune destruction of the beta cells of pancreas, causing an absolute deficiency of insulin secretion. \(^5\)

The pancreatic islets of newly diagnosed patient with type 1 DM show characteristic histological features of autoimmune disease. Islet cell
antibodies (ICA) are frequently present in the plasma (and may be
detectable long before the condition presents clinically). \(^{(1)}\)

This diabetic type is generally related one of more of the following
markers are found in 85-90\% of individuals with fasting hyperglycemia:
islet cell auto antibodies, insulin auto antibodies, glutamic acid
decarboxylase autoantibodies and tyrosine phosphatase 1A-2 and 1A-2B
autoantibodies. \(^{(5)}\)

IDDM accounts for approximately fifteen\% of all diabetic. it occur at any
age but it most common in the young, with a peak incidence between 9
and 14 years of age. \(^{(4)}\)

Only insulin is used to control glucose in type I diabetes. \(^{(9)}\)

Type I DM is common in children, aldosect and young adults < 30 years
of age. these patients present with a triad of polyuria, polydipsia and
polyphagia. The hyperglycemia and the resultant hyperosmolar state (glucose is a hyperosmolar substance) induce an osmotic diuresis leading
to polyuria and obligatory polydipsia to compensate the fluid loss.
Progressive insulin deficiency lead to energy loss. The energy loss in the
form of glycosuria produces weakness. fatigue, weight loss, and general
malsia occur as protein and fat storage are depleted. \(^{(10)}\)

As countrregulatory hormons increase, ketosis results and further
worsening may lead to ketoacidosis characterize by nausea, vomiting,
anorexia, abdominal pain and dehydration. As this point acute worsening
of dehydrating and acidosis can produce symptoms of lethargy, confusion
, stupor and even coma, and the respiratory compensation of metabolic acidosis produces hyperpnea and the deep sighing (kussmaul’ breathing).

"Brittle" diabetes, also known as unstable diabetes or labile diabetes, is a term that was traditionally used to describe dramatic and recurrent swings in glucose levels, often occurring for no apparent reason in insulin-dependent diabetes. This term, however, has no biologic basis and should not be used.

**Diabetes mellitus type II**

It is formerly non-insulin dependent DM (NIDDM) or adult-onset diabetes mellitus is a metabolic disorder characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency.

Type II diabetes accounts for approximately 85% of all diabetics and can occur at any age. It is most common between 40 and 80 years.

Globally, as of 2010, an estimated 285 million people had diabetes, with type II making up about ninety% of the cases. Its incidence is increasing rapidly, and by 2030, this number is estimated to almost double. Diabetes mellitus occurs throughout the world, but is more common (especially type II) in the more developed countries. The greatest increase in prevalence is, however, expected to occur in Asia and Africa, where most patients will probably be found by 2030. The increase in incidence in developing countries follows the trend of urbanization and lifestyle changes, perhaps most importantly a "Western-style" diet.
The effect of diet on glucose control is observed early, before any demonstrable weight loss. Programs that are associated with 5% -10% weight loss in 3 -4 months result in significance improved glycemic control also with exercise and drugs therapy. (9)

Early symptoms of hyperglycemia in type II DM include fatigue, malaise, blurred vision, paresthesias of lower limbs and genitourinary infections. As the disease advances, the triad of polyuria, polydipsia and polyphagia may appear along with weight loss. Most of the patients have one or two complications at the time of diagnosis. As the disease advance the clinical condition gets dominated by complications such as microvascular and macrovascular complications. The untreated patients with type II DM usually do not present in diabetic ketoacidosis. Hyperosmolar non-ketotic diabetic coma is more common in type II untreated diabetes. (10)

**Gestational diabetes mellitus**

Pregnant women who have never had diabetes before but who have high blood sugar (glucose) levels during pregnancy are said to have gestational diabetes. Based on recently announced diagnostic criteria for gestational diabetes, it is estimated that gestational diabetes affects eighteen% of pregnancies. (12)

We don't know what causes gestational diabetes, but we have some clues. The placenta supports the baby as it grows. Hormones from the placenta help the baby develop. But these hormones also block the action of the mother's insulin in her body. This problem is called insulin resistance.
Insulin resistance makes it hard for the mother's body to use insulin. She may need up to three times as much insulin \(^{(12)}\).

**Other specific types of diabetes**

Are associated with certain conditions (secondary) including genetic defects of beta cells function or insulin action, pancreatic disease, disease of endocrine origin, drug or chemical induced insulin receptor abnormalities, and certain genetic syndromes. The characteristics and prognosis of this form of diabetes depend on the primary disorder \(^{(5)}\).

1.1.1.3. **Complications of diabetes mellitus:**

The complication of DM may be divided unto two major categories; acute and chronic. The acute complications are directly related to rapid changes in metabolism and include diabetic ketoacidosis (DKA), hyperosmolar hyperglycemic nonketotic coma (HHNC), and Hypoglycemia. These complications are in part preventable and require immediate therapeutic intervention. The chronic complication, such as vascular disease, nephropathy, neuroathy and altered metabolic milieu of diabetes \(^{(13)}\).

**Acute complications:**

The acute metabolic complications of DM consist of Diabetic ketoacidosis (DKA), hyperosmolar nonketotic coma (HNC), lactic acidosis (LA) and hypoglycemia. The DKA and HNC are related to insulin deficiency. Hypoglycemia results from the treatment of diabetes,
either with oral agent or insulin. Although hypoglycemia may occur in conjunction with oral hypoglycemic therapy, it is more common in patients treated with insulin. LA is usually associated with other factor that may be related to diabetes, such as cardiovascular disease (acute myocardial infarction) associated with hypoxia and excess lactic acid production. \(^{(14)}\)

**Chronic complications:**

The presence of DM immediately increases the risk of developing irreversible clinical complications because of degenerative changes throughout the body. Chronic complication of DM develops primarily in tissues that are affected by high levels of glucose circulating in the blood. And those tissues that require insulin for transport of glucose. Hyperglycemia causes degenerative changes by thickening the basement membrane. Promoting coagulation, obstructing, perfusion including hypoxia and producing tissue necrosis . in those tissue that do not required insulin for glucose transport (e.g. RBCs, Lens, kidney& nerves) the excess of glucose causes fluid to osmotically shift into these cells and causes the cell to rupture \(^{(15)}\).

The chronic complications of diabetes are caused by long terms exposure to glucose, which damages large and small blood vessels and peripheral nerves . macrovascular disease arises when large blood vessels are involved (as in CHD, cerebrovascular disease and peripheral vascular disease) and microvascular disease comprised disorders of the small blood vessels such as retinopathy and nephropathy . Separate metabolic
processes cause damage to the nerve sheath (neuropathy). These chronic complications are all related to duration of diabetes of diabetes and the effectiveness of diabetes control\(^{(16)}\).

1.1.1.4. Skin manifestation of diabetes mellitus:

The human skin is the outer covering of the body. In humans, it is the largest organ of the integumentary system. The skin has multiple layers of ectodermal tissue and guards the underlying muscles, bones, ligaments and internal organs \(^{(17)}\).

Diabetes can affect every part of the body, including the skin. As many as 33 percent of people with diabetes will have a skin disorder caused or affected by diabetes at some time in their lives. In fact, such problems are sometimes the first sign that a person has diabetes. Luckily, most skin conditions can be prevented or easily treated if caught early. \(^{(18)}\).

Cutaneous manifestations in the setting of diabetes can be classified to Non infectious, infectious, related to complication because of vasculopathy and related to complications of diabetes treatment. \(^{(19)}\)

Insulin signaling supports normal skin proliferation, differentiation, and maintenance so in diabetes mellitus there are a variety of cutaneous manifestations. Good metabolic control may prevent some of these manifestations and may support cure. Unfortunately, most glucose-lowering drugs also have cutaneous side effects \(^{(20)}\).
1.1.1.4.1. Non infectious skin manifestation:

Common non infectious skin findings in diabetes include acanthosis nigrican (AN), skin tag, vitiligo, necrobiosis lipodica, diabetic dermopathy (21).

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, and other areas. 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, 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) (22).

Vitiligo is an autoimmune process directly at melanocyte causing depigmentation of the skin. There is usually a symmetrical depigmentation of the skin that often presents on the dorsal of hand and on the face the axillae and genitalia also can be involved (23).

Necrobiosis lipoidica is a disorder of collagen degeneration with a granulomatous response, thickening of blood vessel walls, and fat deposition may be seen in Diabetics. The main complication of the
disease is ulceration, usually occurring after trauma. Infections can occur but are uncommon (24).

Diabetic dermopathy (also known as "shin spots") is a type of skin lesion usually seen in people with diabetes mellitus. It is characterized by dull-red papules that progress to well-circumscribed, small, round, atrophic hyper pigmented skin lesions usually on the shins. It is the most common of several diabetic skin conditions being found in up to 30% of diabetics. Similar lesions can occasionally be found in non-diabetics usually following trauma or injury to the area; however > 4 lesions strongly suggest diabetes (25).

Skin Tags are completely benign skin growth that has no malignant potential. They frequently observed in obese individuals and are known marker for type II Diabetes (26).

1.1.1.4.2. Cutaneous Infection:

Coetaneous Infection occur in 20-50% 0f diabetic patient, more often in those with type 2 diabetes and are often associated with poor glycemic control (19).

Patients with diabetes are at greater risk of infections and of increased severity of infections. (27).

Bacterial infections like Staphylococcus aureus, is the most commom microbe causing skin infection. streptococcal infection are also more frequent in patients with diabetes. (27).
Fungal infection like Candidal infections are more common in diabetes (27).

1.1.1.4.3. **Cueotaneous vasculopathy**

Hyperglycemia causes degenerative changes by thickening the basement membrane. Promoting coagulation, obstructing, perfusion including hypoxia and producing tissue necrosis (15).

1.1.1.4.4. **Cueotaneous reactions of diabetes treatment:**

Insulin-induced disorders in which Insulin allergy may be secondary to insulin molecules, additives, or protein contaminants in the commercial preparation. Local reaction to insulin include erythema, pruritus, indurations at the injection site, subcutaneous nodules. Insulin-induced lipoatrophy is now rare (atrophy of subcutaneous fat) may occur at insulin injections sites 6 to 24 months after initiation of therapy (28).

Reaction to oral hypoglycemic agents like Sulfonylureas are the most common oral hypoglycemic agents that cause skin reactions. About 1-5 % patents taking first-generations sulfonyureas develop coetaneous reactions within 2 months of treatment; generalized erythematous reactions are common and resolve with discontinuations of the medication (29).

1.1.1.5. **Diagnostic criteria with Diabetes Mellitus:**

The diagnostic criteria for diabetes mellitus were modified by the expert committee to allow for earlier detection of the disease. Diagnostic criteria are following (5):
• Random plasma glucose \( \geq 200 \text{ mg/dl (11.1 mmol/L)} \) + symptoms of diabetes

• Fasting plasma glucose \( \geq 126\text{mg/dl (7.0mmol/L)} \)

• Two-hour plasma glucose \( \geq 200 \text{ mg/dl (11.1mmol/L)} \) during an OGTT (75-g glucose load)

An intermediate group who did not meet the criteria of diabetes mellitus but who had glucose level above normal was defined by two methods\(^5\):

• Fasting glucose levels \( \geq 110 \text{ mg/dl but < 126 mg/dl} \) were called the impaired fasting glucose group

• Patients who had 2-hour OGTT levels of \( > = 140 \text{ mg/dl but < 200 mg/dl} \) was defined as impaired glucose tolerance

Hemoglobin A\(1\text{C} \) is a widely used marker of chronic glycemia, reflecting average blood glucose levels over a 2- to 3-month period of time. The test plays a critical role in the management of the patient with diabetes\(^{30}\).

1.1.2. Skin tags (accrochordon):

1.1.2.1. Definition

Skin tags (accrochordon) are extremely common. They are small, benign, flesh colored to hyper pigmented pendunculated skin tags, characteristically attached by short, thin stalk. They are most common on the neck in the axilla and in skin folds. Accrochordons are more frequent in the obese. They are uncommon before thirty years of age. Accrochordons can be treated by simple excision with scissors by electrodescication, or using cryotherapy\(^{31}\).
1.1.2.2. Clinical findings:

Skin tags can be found throughout the adult population. They have no sex or race predilection. They are completely benign skin growth that has no malignant potential. Skin tags are almost never seen in children. Most skin tags are minute 1 to 5 mm in length, with a skin-colored to slightly hyper pigmented appearance\(^{(32)}\).

The lesion develop on the skin surface that rub together or that chronically rub against clothes\(^{(33)}\).

1.1.2.3. Histology:

Skin tag histological classify as fibromas with hyperplasic epidermis connected to the skin on connective tissue stalk\(^{(33)}\).

The overlying epidermis is essentially normal. The skin tag appears as an outgrowth of the skin. The dermis appears normal, and there is a minimal inflammatory infiltrate present\(^{(32)}\).

1.1.3. Pathophysiology of Skin Tags:

Both insulin and IGF-1 stimulate the synthesis of androgens in the ovaries and testis and both inhibit hepatic synthesis of sex hormone binding globulin (SHBG), allowing for higher level of free biologically active androgens, which directly contribute to the pathophysiology of (coetaneous papilloma (skin tag))\(^{(26)}\).

Skin Tags are characterized by hyper keratinization. Chronic hyperinsulinemia leads to chronic elevation of non-estratified FFAs, which causes increased production of epidermal growth factor and
decrease in production of IGFBP-3 locally, allowing an increase in free IGF-1 that promotes the proliferation of keratinocytes, furthermore, decreased IGFBP-3 reduces the binding affinity of retinoic acid for its receptors, thus reducing the normal inhibition of cellular proliferation (26).

In summary, a high calorie, high-GL diet generate constant metabolic cascade:

Hyperinsulimemia → Insulin resistance → decreases IGFBP-1 production → increase circulating free IGF-1 → cellular hypertrophy and cell proliferation (26)
1.2. Literature review:

Many current researches and studies in different countries and nations assess the association between the skin tags and Diabetes Mellitus.

In Europe 1987 the study was conducted in which the skin tag serve as marker for DM. which Two hundred and sixteen non hospitalized patients with skin tags (ST) were studied for the presence of diabetes mellitus (DM) and obesity. Overt DM was found in 57 (26.3%) patients and impaired glucose tolerance test was found in 17 (7.9%) patients. Sixteen new cases of DM (6%) were found among this group. All the diabetic patients in the study population had non-insulin dependent DM. Sixty-two (28.7%) of the patients were obese. No correlation was found between the localization, size, color and number of the ST and the presence of DM. this study indicates that ST are not associated with increased incidence of obesity compared to the general population. On the other hand, ST are associated with impaired carbohydrate metabolism, and may serve as means for identifying patients at increasing risk of having DM\(^{(34)}\).

In an Epidemiological study in India. 22-oct-1995 where 35 patients with ST were screened out of 5000 consecutive patients visiting dermatology clinic to ascertain whether skin tags (ST) are associated with a higher risk for diabetes mellitus (DM). The study group ranged in age from 35 to 73 years, of the cases, 62.8% (22 patients) had DM. Four new cases of DM (11.4%) were found among this group. All the diabetic patients in this study population had noninsulin dependent DM, The frequency of DM in
ST patients was found to increase with age; however, it was statistically insignificant. No correlation was found between localization, size, color, or number of ST and the presence of DM. This study confirmed that the frequency with which ST had been found to co-exist with DM in this population is significant, and ST may serve as a marker for DM\textsuperscript{(35)}.

In Turkey at June 2002 there was another study that evaluated 120 patients with acrochordon for the presence of impaired carbohydrate metabolism. Overt diabetes mellitus (DM) was found in (73.3\%) 88 patients, glucose intolerance was detected in(5\%) 6 patients and (3.3\%) 4 patients had reactive hypoglycemia. It was concluded that acrochordons may be skin markers of underlying impaired carbohydrate metabolism and the patients with acrochordon should be evaluated for the presence of diabetes mellitus\textsuperscript{(36)}.

In Tehran, Iran at nov.2007 A case-control study was conducted in individuals over 15 years old, comparing cases (n = 104) with at least three skin tags and age-, sex-, and body mass index (BMI)-matched controls (n = 94) without skin tag. Cases and controls were recruited from patients consecutively seen at an academic outpatient dermatology clinic. All patients underwent a standard 2-h oral glucose tolerance test with 75 g glucose. The result of this study was that Patients with skin tag had higher frequency of diabetes than the control group (23.07\% vs. 8.51 \%). The difference in the frequency of IGT was not significant (13.46\% vs. 10.63\%), there was a positive correlation between the total number of skin tags and the mean fasting plasma glucose, and patients with more than 30 skin tags were particularly at an increased risk of diabetes (52.0\%). No
correlation was found between the number of skin tags and BMI. They did not find any correlation between the anatomical localization of skin tags and impaired carbohydrate metabolism, except for skin tags under the breast in women. These results show an increased risk of diabetes mellitus in patients with multiple skin tags. With regard to the importance of early diagnosis of diabetes, we recommend a high level of suspicion for impaired carbohydrate metabolism in patients with skin tag \(^{(37)}\).

In Germany 2008, there was another study involved the following. Clinical and metabolic glucose/insulin characteristics of men with multiple (8 or more) skin tags on the neck were compared with a control group with few or none. Both groups were divided in two subgroups according to normal or abnormal laboratory findings. In the study subgroup with normal laboratory findings, the number of skin tags varied from 8-33, whereas in those with abnormal laboratory findings, the range was 9-65. Eight or more skin tags were related with statistically significant laboratory glucose/insulin abnormalities: basal hyperinsulinemia (p<0.002), postprandial hyperinsulinemia (p<0.003), and postprandial hyperglycemia (p<0.01). In the multiple skin tag group 77% had diverse laboratory abnormalities, including insulin resistance, basal hyperinsulinemia, postprandial hyperinsulinemia, glucose intolerance or type 2 diabetes, in contrast with the control group, where only 33% showed laboratory abnormalities. One-third of the study group had acanthosis nigricans. Only 15% of patients with metabolic abnormalities did not show any cutaneous expression of glucose/insulin alterations (9 or more skin tags on the neck, acanthosis nigricans, or waist
circumference greater than 95 cm). Multiple skin tags were more sensitive than acanthosis nigricans in identifying those with alterations in the glucose/insulin metabolism (77 vs. 32 % respectively), although less specific (68 vs. 100%). Multiple skin tags should raise suspicion of insulin resistance or hyperinsulinemia (38).

In Brasil 2010 a cross-sectional study involving adult patients receiving care at a university teaching hospital was conducted to evaluate the association between skin tags in the neck or axillary regions and insulin resistance. Cases were defined as patients with > 5 skin tags in the neck region and/or axilla. Insulin resistance was estimated using the HOMA-IR index. Results were adjusted for the other known covariates of risk for insulin resistance using a multiple logistic regression model. Ninety-eight cases and 103 controls were evaluated. There was no difference between the groups with respect to age or gender. Skin tags were directly associated with HOMA-IR values (odds ratio = 1.4), hypertriglyceridemia and body mass index, irrespective of adjustment for diabetes mellitus, age, skin phototype, gender, family history of diabetes mellitus or hip/waist ratio. Qualitatively elevated HOMA-IR levels (>3.8) were also significantly associated (odds ratio = 7.5). The presence of multiple skin tags was strongly associated with insulin resistance irrespective of other risk factors (39).

In Iran 2012 other study in the same task in whether there is association between skin tag and diabetes mellitus. This study was carried out on 80 patients with skin tags as a case group and 80 patients without skin tags as a control group that they were referred to Semnan dermatological clinics.
Then fasting blood sugar (FBS) were checked out in both two groups. In addition, height and weight were measured in all patients and body mass index (BMI) calculated for each of the patient. Results: 43.8% and 55% of patients were respectively female in the case group and the control group. Age mean (± SD) was 44.3±16.6 and 37.3±18.9 years in the case and control group, respectively. BMI mean (±SD) index was 28.0±4.3kg/m² in the patients with skin tag, whereas, it was 25.5±5.1 kg/m² in the patients without skin tag (P=0.001). Patients with skin tag had higher frequency of diabetes than patients in the control group (27.5% vs. 5%) and also the case group showed a higher frequency of pre diabetes than the control group (20% vs. 15%). The probability of presence of diabetes mellitus in the patients with skin tag was 6.82 times more than the patients in the control group (Odds ratio=6.82, 95% Confidence interval: 2.06-22.56, P=0.002). These data suggest that there was an association between skin tag and diabetes mellitus. Therefore, screening of patients with skin tag is recommended for early diagnosis diabetes mellitus (40).
1.3. **Rational and justification:**

Diabetes mellitus is a heterogenous condition reflecting different metabolic disorders and accompanied by a variety of complications. However, it is hyperglycaemia that is the common feature and this is used to define diabetes. Diabetes was previously considered a disease of minor significance to world health. However, there has been an explosive increase in the number of people diagnosed with diabetes worldwide in the last few decades.

Skin is the largest system in the body can reflect many metabolic disorders; so assist early diagnosis.

Most Sudanese people are not aware of the skin tags because they are harmless and painless unless they are inflamed or irritated, but other consider them as ugly so remove them for cosmetic purposes regardless of the causes of their appearance.

This study can assist dermatologist to evaluate the patients with acrochordons for the presence of diabetes mellitus.

This may be one of the first studies in Sudan that correlate skin tags and diabetes mellitus.
1.4. Objectives:

1.4.1. General objective:
To estimate the prevalence of hyperglycemia among patients with acrochordons (Skin Tags) in Khartoum state.

1.4.2. Specific objectives:
1. To measure fasting blood Glucose (FBG) in patients with Skin Tags.
2. To estimate the prevalence of hyperglycemia among patients with Skin Tags.
3. To correlate fasting blood Glucose with numbers of Skin Tags.
4. To correlate the effect of age with number of Skin Tags.
5. To correlate the effect of gender with number of Skin Tags.
Chapter two

Materials

And

Methods
2. Materials and methods

2.1. Study approach

2.1.1. Study area:

Khartoum state

2.1.2. Study duration:

Three months (Dec 2012 - Mar 2013)

2.1.3. Study design:

Cross sectional descriptive study conducted.

2.1.4. Study population:

The study population comprised Ninety six Sudanese patients, with different ages and gender randomly selected with at least 3 skin tags

2.2. Inclusion Exclusion criteria:

2.2.1. Inclusion criteria:

Patient with at least three benign clinically diagnosed skin tags

2.2.2. Exclusion criteria:

Pregnant women, acromegly, poly cystic ovary syndrome, insulinoma, drugs that induced hyperinsulinemia and hereditary skin tags were excluded (see Appendix I)
2.3. Ethical approval

All patients included in this study were aware about the purpose of the study.

2.4. Sampling:

2.4.1. Sample size:

Ninety six fasting blood samples were collected.

2.4.2. Samples collection:

Under a septic condition Fasting Venous blood will be collected in fluoride oxalate container. About 2.5 ml venous blood will be collected from all participants after fasting 8 - 12 hour fast (overnight) by using disposable syringes from the anticubital vein. Water is not a factor, so the person can consume any amount of water, but no foods, or other liquids, after cleaning the skin with 70% alcohol. Then drawn specimens poured slowly into fluoride oxalate container, and separated by centrifugation at 3200 rpm for three minutes.

2.5. Methodology:

Fasting blood Sugar was measured using commercially made kits.

2.5.1. Method of glucose estimation:

Glucose oxidase method was used (see Appendix IV).
2.5.1.1. Principle of the method:

Glucose oxidase (GOD) catalyses the oxidation of glucose to gluconic acid. The formed hydrogen peroxide (H2O2), is detected by a chromogenic oxygen acceptor, phenol-aminophenazone in the presence of peroxidase (POD):

**Principle:** (Trinder’s method)

- D-glucose +H2O+O2 → D-glucose
- D-glucose +H2O+O2 → Glucose oxidase +D-gluconic acid+H2O2
- H2O2+ 4-aminophenazone+phenol → Peroxidase + Quinonemine +4 H2O

The intensity of the color formed is proportional to the glucose concentration in the sample.

2.5.1.2. Reference values of fasting blood Sugar:

- The FPG (fasting plasma Sugar) test
  - at least 126 mg/dl diabetes
  - between 110 mg/dl and 125.99 mg/dl impaired FBG
  - less than 110 mg/dl means normal

2.5.2. Instrument:

**Colorimeter**

Serial No. 558, factory: Lab Tech, country: india. (see Appendix III)
2.6. **Quality control:**

For internal quality control, normal control sera (normal spintrol) and pathological control sera (pathological spintrol) were included within every batch of chemical analysis. (see Appendix V) Results +/- 2sd were accepted.

2.7. **Statistical analysis:**

SPSS version 16 was used to analyze Data.
Chapter three

Results
3. **Results:**

Fasting blood Glucose of ninety six patients with at least three accrochordons (Skin Tags) was measured.

In this study the overall abnormal fasting blood sugar level were 65 (67.7%), while 31 (32.3%) were normal. Among the abnormal FBS there were 44 (45.8%) diabetics and 21 (21.9%) were impaired FBS according WHO criteria (Figure no 3.1).

The mean of Fasting Blood Sugar levels in Normal (90 mg/dL), Impaired (117 mg/dL) and Diabetics (197 mg/dL) (figure no 3.2).

The Correlation between Fasting Blood Sugar levels and number of Skin Tags is highly significant (p=0.001) (table no 3.1)

The most frequent localization of acchrochordons were face and neck (17.7%) (Skin Tags) (Table no 3.2)

The effect of age on Skin Tags is highly significant (p= 0.000) (table no 3.3)

The effect of gender on skin tags is not significant (p=0.547) (table no 3.4)
Figure No. (3.1): The prevalence of Diabetes Mellitus and impaired Fasting blood Sugar in patient with Skin Tags.
Figure No. (3.2) fasting Blood Sugar's mean:
**Table No** (3.1). The Correlation between Fasting Blood sugar levels and number of Skin Tags

<table>
<thead>
<tr>
<th></th>
<th>tag numbers</th>
<th>Fasting blood Glucose</th>
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</thead>
<tbody>
<tr>
<td><strong>tag numbers</strong></td>
<td>Pearson Correlation</td>
<td>1</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td></td>
<td>96</td>
</tr>
<tr>
<td><strong>N</strong></td>
<td></td>
<td>96</td>
</tr>
<tr>
<td><strong>Fasting blood</strong></td>
<td>Pearson Correlation</td>
<td>.346**</td>
</tr>
<tr>
<td>Glucose</td>
<td>Sig. (2-tailed)</td>
<td>.001</td>
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<tr>
<td><strong>N</strong></td>
<td></td>
<td>96</td>
</tr>
</tbody>
</table>

Sig. (*p* value= 0.001)
**Table No. (3.2):** localizations of Skin Tags:

<table>
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<tr>
<th>Location</th>
<th>Number of patients</th>
<th>Percent %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Face only</td>
<td>15</td>
<td>15.6</td>
</tr>
<tr>
<td>Neck only</td>
<td>15</td>
<td>15.6</td>
</tr>
<tr>
<td>Axilla only</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Face and neck</td>
<td>17</td>
<td>17.7</td>
</tr>
<tr>
<td>face and axilla</td>
<td>8</td>
<td>8.3</td>
</tr>
<tr>
<td>Neck and axilla</td>
<td>2</td>
<td>2.1</td>
</tr>
<tr>
<td>Face , neck and axilla</td>
<td>6</td>
<td>6.3</td>
</tr>
<tr>
<td>Mixed</td>
<td>26</td>
<td>27.1</td>
</tr>
<tr>
<td>Others</td>
<td>7</td>
<td>7.3</td>
</tr>
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</table>
Table No. (3.3): The effect of age on Skin Tags:

Correlations

<table>
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<tr>
<th></th>
<th>age of patient</th>
<th>tag numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age of patient</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pearson Correlation</td>
<td>1</td>
<td>.431**</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td></td>
<td>.000</td>
</tr>
<tr>
<td>N</td>
<td>96</td>
<td>96</td>
</tr>
<tr>
<td><strong>Tag numbers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pearson Correlation</td>
<td>.431**</td>
<td>1</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>.000</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>96</td>
<td>96</td>
</tr>
</tbody>
</table>

Sig. ($p$ value = 0.000)
Table No. (3.4): The effect of gender on Skin Tags:

<table>
<thead>
<tr>
<th>tag numbers</th>
<th>Sum of Squares</th>
<th>df</th>
<th>Mean Square</th>
<th>F</th>
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</thead>
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<tr>
<td>Between Groups</td>
<td>22.102</td>
<td>1</td>
<td>22.102</td>
<td>.365</td>
</tr>
<tr>
<td>Within Groups</td>
<td>5697.304</td>
<td>94</td>
<td>60.610</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>5719.406</td>
<td>95</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sig. (p value = 0.547)
Chapter four

Discussion
1.1. Discussion:

Since an association between acrochordons and Diabetes Mellitus was mentioned by Kahana 1987\(^{34}\). Different studies concerning this relation have been reported.

Among these diabetic patients there were 41 (93.2%) previously diagnosed and 3 (6.8%) cases newly discovered and among patients with impaired FBS there were 15 (71.4%) previously diagnosed and 6 (28.6%) newly discovered.

The most frequent localization of acrochordons was face and neck.

The correlation between Fasting Blood Sugar and number of Skin Tags is highly significant (p=0.001) and this agrees with Abbas Rasi\(^{37}\).

In this study all patients previously diagnosed had (NIDDM) so we proposed that acrochordons in the patients may be consequence of underlining insulin resistance which is frequently accompanied by an increase circulating insulin level, this agree with Sudy\(^{39}\) and Tamega\(^{38}\).

There is a significant correlation between age and number of skin tags (p=0.000) and this agrees with Thappa\(^{35}\), and disagree with Tamega\(^{38}\).

There is no significant association between skin tag and gender (p=0.547) and this agree with Tamega\(^{38}\).
1.2. Conclusion:

There was an association between Skin Tags and Diabetes Mellitus and the presence of them can be marker for diabetes mellitus

There was newly cases discovered with diabetes mellitus and impaired fasting blood sugar

1.3. Recommendations:

1. Patients with acrochordon (Skin Tags) should have been screened for the presence of Diabetes Mellitus.
2. Insulin level should be measured in patients with acrochordons.
3. More studies should be done to approve this relationship.
References
References:


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Appendix I:

بسم الله الرحمن الرحيم

University of Khartoum

Faculty of Medical Laboratory Sciences

Department of Chemical Pathology

Questionnaire

Patient name .................................................. lab NO ..........
Age ..............................................................
Gender Male ( ) female ( )
Numbers of Skin Tags ........................................
Locations ......................................................
Previously diagnosed with …. Diabetes ( ) pridiabetes ( ) none ( )
Type .......

Pregnant ( ) acromegly ( )
hereditary skin tags ( ) insulinoma ( )
poly cystic ovary syndrome ( )

drugs :

glucocorticoids ( ) niacin ( )
oral contraceptives ( ) insulin ( )

Telephone NO ..............................................

Signature ...............................................
Appendix II:

accrochordons (skin tags):
Appendix III:

Colorimeter
Appendix IV:

Glucose oxidase method

Appendix V:

Normal and pathological control sera
Quantitative determination of glucose

IVD

Store at 2-8°C

PRINCIPLE OF THE METHOD
Glucose oxidase (GOD) catalyses the oxidation of glucose to gluconic acid. The formed hydrogen peroxide (H₂O₂) is detected by a chromogenic oxygen acceptor, phenol-aminophenazone in the presence of peroxidase (POD):

\[ \beta-D-Glucose + O_2 + H_2O \xrightarrow{\text{GOD}} \text{Gluconic acid} + H_2O_2 \]

H₂O₂ + Phenol + Aminophenazone \xrightarrow{\text{POD}} \text{Quinone} + H₂O

The intensity of the color formed is proportional to the glucose concentration in the sample.

CLINICAL SIGNIFICANCE
Glucose is a major source of energy for most cells of the body; insulin facilitates glucose entry into the cells. Diabetes is a disease manifested by hyperglycemia; patients with diabetes demonstrate an inability to produce insulin. Clinical diagnosis should not be made on a single test result; it should integrate clinical and other laboratory data.

REAGENTS

<table>
<thead>
<tr>
<th>R 1</th>
<th>Buffer</th>
<th>TRIS pH 7.4</th>
<th>92 mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Phenol</td>
<td>0.3 mmol/L</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>R 2</th>
<th>Glucose oxidase (GOD)</th>
<th>15000 U/L</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Peroxidase (POD)</td>
<td>100 U/L</td>
</tr>
<tr>
<td></td>
<td>4-Aminophenazone (4-AP)</td>
<td>2.6 mmol/L</td>
</tr>
</tbody>
</table>

GLUCOSE CAL
Glucose aqueous primary standard 100 mg/dL

PREPARATION
Working reagent (WR): Dissolve (→) the contents of one vial R 2 in one bottle of R 1 Buffer. Cap and mix gently to dissolve contents. The reagent is stable 1 month after reconstitution in the refrigerator (2-8°C) or 7 days at room temperature (15-25°C).

STORAGE AND STABILITY
All the components of the kit are stable until the expiration date on the label when stored tightly closed at 2-8°C, protected from light and contaminations prevented during their use. Do not use reagents over the expiration date.

Signs of reagent deterioration:
- Presence of particles and turbidity.
- Blank absorbance (A) at 505 nm ≥ 0.10.

ADDITIONAL EQUIPMENT
- Spectrophotometer or colorimeter measuring at 505 nm.
- Matched cuvettes 1.0 cm light path.
- General laboratory equipment.

SAMPLES
Serum or plasma, free of hemolysis and CSF.

PROCEDURE
1. Assay conditions:
   - Wavelength: 505 nm (490-550)
   - Cuvette: 1 cm light path
   - Temperature: 37°C / 15-25°C
2. Adjust the instrument to zero with distilled water.
3. Pipette into a cuvette:

<table>
<thead>
<tr>
<th>WR (mL)</th>
<th>Blank</th>
<th>Standard</th>
<th>Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

4. Mix and incubate for 10 min at 37°C or 20 min at room temperature (15-25°C).

5. Read the absorbance (A) of the samples and standard, against the Blank. The color is stable for at least 30 minutes.

CALCULATIONS
(A) Sample \times 100 (Standard conc.) = mg/dL glucose in the sample
(A) Standard

Conversion factor: mg/dL x 0.0555 = mmol/L

QUALITY CONTROL
Control sera are recommended to monitor the performance of assay procedures. "SPINTROL FT NORMAL and PATHOLOGIC" (Ref: 10027120 and 10022110).

If control values are found outside the defined range, check the instrument, reagents and calibrator for problems.

Each laboratory should establish its own Quality Control scheme and corrective actions if controls do not meet the acceptable tolerances.

REFERENCE VALUES
Serum or plasma: 60 – 110 mg/dL = 3.33 – 6.10 mmol/L
CSF: 60 – 80% of the blood value

These values are for orientation purpose; each laboratory should establish its own reference range.

PERFORMANCE CHARACTERISTICS
Measuring range: From detection limit of 0.04 mg/dL to linearity limit of 500 mg/dL.

If the results obtained were greater than linearity limit, dilute the sample 1/2 with NaCl 9 g/L and multiply the result by 2.

Precision:

<table>
<thead>
<tr>
<th>Mean (mg/dL)</th>
<th>Intra-assay (n=20)</th>
<th>Inter-assay (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>96.4</td>
<td>96.4</td>
<td>248</td>
</tr>
<tr>
<td>1.55</td>
<td>1.58</td>
<td></td>
</tr>
<tr>
<td>0.83</td>
<td>1.43</td>
<td></td>
</tr>
<tr>
<td>0.59</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sensitivity: 1 mg/dL = 0.0036 A.

Accuracy: Results obtained using SPINREACT reagents (y) did not show systematic differences when compared with other commercial reagents (x). The results obtained using 50 samples were the following:

Correlation coefficient (r): 0.99.
Regression equation: y = 1.0x + 0.12.

The results of the performance characteristics depend on the analyzer used.

INTERFERENCES
Haemoglobin up to 4 g/L, bilirubin up to 20 mg/dL, creatinine up to 100 mg/dL and gallactose up to 1 g/L do not interfere.

A list of drugs and other interfering substances with glucose determination has been reported by Young et al.

NOTES
1. GLUCOSE CAL: Proceed carefully with this product because due its nature it can get contaminated easily.
2. Calibration with the aqueous standard may cause a systematic error in automatic procedures. In these cases, it is recommended to use a serum Calibrator.
3. Use clean disposable pipette tips for its dispensation.
4. SPINREACT has instruction sheets for several automatic analysers. Instructions for many of them are available on request.

BIBLIOGRAPHY

PACKAGING
Ref:1001190 4 x 125 mL
Ref:1001191 4 x 250 mL
Ref:1001192 10 x 50 mL
## Electrolios / Electrolytes

<table>
<thead>
<tr>
<th>Component</th>
<th>método</th>
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<th>Rango</th>
<th>Unidad</th>
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</thead>
<tbody>
<tr>
<td>Calcio (Ca)</td>
<td>o-Cresoltartaleina-complexona</td>
<td>4,65</td>
<td>4,09 - 5,21</td>
<td>mEq/L</td>
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<td>Calcium (Ca)</td>
<td>o-Cresolphosphate-complex</td>
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<td>2,05 - 2,60</td>
<td>mmol/L</td>
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<td></td>
<td></td>
<td>9,30</td>
<td>8,18 - 10,42</td>
<td>mg/dL</td>
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<tr>
<td>Cloruros (Cl)</td>
<td>Método colorimétrico</td>
<td>100</td>
<td>88 - 112</td>
<td>mmol/L</td>
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<td>Molybdate-UV</td>
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<tr>
<td>Litio (Li)</td>
<td>Método Colorimétrico</td>
<td>0,84</td>
<td>0,74 - 0,94</td>
<td>mg/dL</td>
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<tr>
<td>Lithium (Li)</td>
<td>Colorimetric method</td>
<td>1,21</td>
<td>1,07 - 1,35</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Magnesio (Mg)</td>
<td>Calmagila</td>
<td>2,20</td>
<td>1,82 - 2,58</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Magnesium (Mg)</td>
<td>Kalmagile</td>
<td>0,92</td>
<td>0,76 - 1,07</td>
<td>mmol/L</td>
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<tr>
<td>Potasio (K)</td>
<td>I.S.E. Potenciometría indirecta</td>
<td>4,35</td>
<td>3,92 - 4,78</td>
<td>mEq/L</td>
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<tr>
<td>Potassium (K)</td>
<td>I.S.E. Indirect potentiometry</td>
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<tr>
<td>Sodio (Na)</td>
<td>I.S.E. Potenciometría indirecta</td>
<td>140</td>
<td>125 - 155</td>
<td>mmol/L</td>
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<tr>
<td>Sodium (Na)</td>
<td>I.S.E. Indirect potentiometry</td>
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<td>mEq/L</td>
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## Sustratos / Sustrates

<table>
<thead>
<tr>
<th>Component</th>
<th>método</th>
<th>Valor</th>
<th>Rango</th>
<th>Unidad</th>
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<tbody>
<tr>
<td>Ácido Urico</td>
<td>Uricasa-PAP</td>
<td>5,77</td>
<td>5,07 - 6,47</td>
<td>mg/dL</td>
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<tr>
<td>Uric Acid</td>
<td>Uricase-PAP</td>
<td>343</td>
<td>302 - 385</td>
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<tr>
<td>Bicarbonato</td>
<td>Enzimático</td>
<td>20,4</td>
<td>16,0 - 24,8</td>
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<tr>
<td>Bicarbonate</td>
<td>Enzymatic</td>
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<tr>
<td>Bilirrubina TOTAL</td>
<td>Jendrassik</td>
<td>1,84</td>
<td>1,52 - 2,16</td>
<td>mg/dL</td>
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<tr>
<td>TOTAL Bilirubin</td>
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<td>26,0 - 36,8</td>
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<td>Bilirrubina DIRECTA</td>
<td>Jendrassik</td>
<td>1,03</td>
<td>0,85 - 1,21</td>
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<td>DIRECT Bilirubin</td>
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<td>17,6</td>
<td>14,6 - 20,6</td>
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<tr>
<td>Creatinina</td>
<td>Jaffé sin desproteinización</td>
<td>1,50</td>
<td>1,29 - 1,71</td>
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<td>Creatinine</td>
<td>Jaffé without deproteinization</td>
<td>133</td>
<td>114 - 151</td>
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<td>Glucosa</td>
<td>Hexokinasa / GOD</td>
<td>113</td>
<td>97 - 129</td>
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<td>Glucose</td>
<td>Hexokinase / GOD</td>
<td>6,26</td>
<td>5,35 - 7,18</td>
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<td>Enzimático-colorimétrico</td>
<td>40,5</td>
<td>35,8 - 45,2</td>
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<td>Enzymatic-colorimetric</td>
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<td>5,96 - 7,52</td>
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<td>Componente / Component</td>
<td>Método / Method</td>
<td>Valor / Value</td>
<td>Rango / Range</td>
<td>Unid. / Units</td>
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<td>Electrolitos / Electrolytes</td>
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<tr>
<td>Calcio (Ca) / Calcium (Ca)</td>
<td>o-Cresol-benzena-complexo / o-Cresolphtalaein-complex</td>
<td>6.25</td>
<td>5.50 - 7.00</td>
<td>mEq/L / mmol/L</td>
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<td>3.13</td>
<td>2.75 - 3.50</td>
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<td>12.5</td>
<td>11.0 - 14.0</td>
<td>mmol/L / mEq/L</td>
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<td>Cloruros (Cl) / Chloride (Cl)</td>
<td>Método colorimétrico / Colorimetric method</td>
<td>110</td>
<td>97 - 123</td>
<td>mg/dL / mEq/L</td>
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<tr>
<td>Hidrógeno (H) / Hydrogen (H)</td>
<td>Ferrozine</td>
<td>192</td>
<td>163 - 221</td>
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<td>Hierro (Fe) / Iron (Fe)</td>
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<td>34.4</td>
<td>29.3 - 39.6</td>
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<tr>
<td>Fosfato inorgánico (P) / Inorganic Phosphorus (P)</td>
<td>Molibdato-UV / Molybdate-UV</td>
<td>6.98</td>
<td>6.03 - 7.88</td>
<td>mg/dL / mmol/L</td>
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<td>2.25</td>
<td>1.96 - 2.54</td>
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<td>Litio (Li) / Lithium (Li)</td>
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<td>1.22 - 1.54</td>
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<td>Magnesio (Mg) / Magnesium (Mg)</td>
<td>Calmagita / Kalmagite</td>
<td>3.45</td>
<td>2.66 - 4.04</td>
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<td>1.44</td>
<td>1.19 - 1.66</td>
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<tr>
<td>Potasio (K) / Potassium (K)</td>
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<td>6.35</td>
<td>5.73 - 6.97</td>
<td>mmol/L / mEq/L</td>
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<tr>
<td>Sodio (Na) / Sodium (Na)</td>
<td>I.S.E. Potenciometría indirecta / I.S.E. Indirect potentiometry</td>
<td>142</td>
<td>127 - 152</td>
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<td>Zinc (Zn) / Zinc (Zn)</td>
<td>Color 5-Br PAPS</td>
<td>117</td>
<td>102 - 132</td>
<td>mg/dL / μmol/L</td>
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<table>
<thead>
<tr>
<th>Sustratos / Sustrates</th>
<th></th>
<th></th>
<th></th>
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<tbody>
<tr>
<td>Ácido Úrico / Urinary Acid</td>
<td>Uricasa-PAP / Uricase-PAP</td>
<td>8.95</td>
<td>7.87 - 10.03</td>
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<td>533</td>
<td>468 - 597</td>
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<td>Bicarbonato / Bicarbonate</td>
<td>Enzimático / Enzymatic</td>
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<td>26.5 - 41.3</td>
<td>mmol/L / mg/dL</td>
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<tr>
<td>Bilirrubina TOTAL / TOTAL Bilirubin</td>
<td>Jendrassik</td>
<td>5.00</td>
<td>4.14 - 5.86</td>
<td>mg/dL / mmol/L</td>
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<td>85.3</td>
<td>70.6 - 99.9</td>
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<td>Bilirrubina DIRECTA / DIRECT Bilirubin</td>
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<td>2.14 - 3.02</td>
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<tr>
<td>Creatinina / Creatinine</td>
<td>Jaffe sin desproteínización / Jaffe without deproteinization</td>
<td>5.15</td>
<td>4.44 - 5.86</td>
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<td>Glucosa / Glucose</td>
<td>Hexokinasa / GOD</td>
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<td>15.4</td>
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<tr>
<td>Urea / Urea</td>
<td>Enzimático-colorimétrico / Enzymatic-colorimetric</td>
<td>127</td>
<td>112 - 142</td>
<td>mg/dL / mmol/L</td>
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<td>21.1</td>
<td>18.7 - 23.6</td>
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