Republic of Iraq
Ministry of Higher Education and Scientific Research
University of Diyala - College of Medicine

Cutaneous Complications of Insulin Therapy in Type I Diabetic Children Attending Al-Batool Teaching Hospital

A graduation project
submitted to College of Medicine - University of Diyala
in partial fulfillment of the
requirements for the degree of
Bachelor of Medicine, Bachelor of Surgery (MBChB)

By

Salman Mahdi Salman

Supervised by

Dr. Mohammad Kassem Saleh

MBChB, MSc Medical Microbiology

Department of Family and Community Medicine, College of Medicine,
University of Diyala

2022-2023

بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

(وَمَا أُوتِيتُم مِّنَ الْعِلْمِ إِلَّا قَلِيلًا)

صَدَقَ اللَّهُ الْعَظِيْم

سورة الإسراء

الآية ٨٥

Supervisor Certification

I hereby certify that this graduation project entitled **(Cutaneous Complications of Insulin Therapy in Type I Diabetic Children Attending Al-Batool Teaching Hospital)** by **(Salman Mahdi Salman)** was prepared under my supervision at Department of Family and Community Medicine, College of Medicine, University of Diyala, in partial fulfillment of the requirements for the degree of Bachelor of Medicine, Bachelor of Surgery (MBChB).

Supervisor
Dr. Mohammad Kassem Saleh
MBChB, MSc Medical Microbiology

/ / 2023

Prof. Dr. Ismail Ibrahim Latif
Dean of College of Medicine - University of Diyala

/ / 2023

Dedication

I dedicate this study to my father, my mother and everyone who wants to benefit from this study.

Acknowledgements

Praise be to Allah, The Most Merciful, The Most Compassionate, for the guidance, strength, power of mind, protection and skills, and for giving me a healthy life.

I am greatly indebted to my supervisor Dr. Mohammad Kassem Saleh for his moral and scientific support and kind cooperation and useful continuous advices throughout my work and preparation for this graduation project.

Summary

Diabetes Mellitus is characterized by hyperglycemia and glycosuria and occurs as a common end point of many disease processes. The most common type occurring in childhood is type I diabetes mellitus (DM1), which is caused by autoimmune destruction of the pancreas. Patients with DM1 have severe and usually permanent insulin deficiency and require insulin for survival and prevention of life-threating episodes of ketoacidosis.

The cutaneous complications of insulin therapy include: skin lipohypertrophy, skin lipoatrophy, allergy and others.

The current study aims to:

1. Determine the prevalence of the various cutaneous complications of insulin therapy in insulin dependent diabetes mellitus.
2. Explore the factors that may affect the development of such complications.
3. Assess the implications of having such complications on the general condition of the child.

This cross-sectional study recruited 102 patients with type I diabetes mellitus (with a male to female ratio of 1:1.3) who were attending the outpatient diabetes clinic at Al-Batool Teaching Hospital, Diyala, Iraq, over a period of three months from the first of November, 2022 to the first of February, 2023, and assessed them for the presence of cutaneous complications of insulin therapy.

The cutaneous complications were found in 55.9% of patients and the most common complication was lipohypertrophy of the skin (93%), whereas allergy to insulin was reported in 7% of patients, while lipoatrophy and other cutaneous complications were not reported. Other non-cutaneous complications of diabetes mellitus were found to be more prevalent among patients with cutaneous complications.

Most of these cutaneous complications were found to occur in the upper arms as they are the usual insulin injection sites, and more frequently in those who either did not change or occasionally changed the injection site, and also in those using wrong injection technique; all these are either because of poor education or failure to follow the instructions, as the academic achievement of the person who injects the insulin had no role.

So, proper education about insulin injection sites and technique and the maintenance of this education is the key to prevent the development of these cutaneous complications.

Introduction

Diabetes Mellitus is characterized by hyperglycemia and glycosuria and occurs as a common end point of many disease processes. The most common type occurring in childhood is type I diabetes mellitus (DM1), which is caused by autoimmune destruction of the pancreas. Patients with DM1 have severe and usually permanent insulin deficiency and require insulin for survival and prevention of life-threating episodes of ketoacidosis [1].

The incidence and prevalence of all types of diabetes mellitus is increasing at an alarming rate. Modern therapy involves greater and earlier use of intensive insulin regimens in order to achieve better control of blood glucose levels and reduce the long-term risks associated with the condition. Insulin therapy is associated with important cutaneous adverse effects, which can affect insulin absorption kinetic causing glycemic excursion above and below target levels for blood glucose [2].

Insulin

The beta cells of the pancreas (in areas called the islets of langerhans) make the insulin. When the body cannot make enough insulin on its own, as in DM1, the person needs to inject insulin made from other sources, i.e., beef, pork, or human insulin (of recombinant DNA origin or pork-derived, semisynthetic).

There are areas of the outer part of the cell that allow the cell to join or bind with insulin that is in the blood. When the cell and insulin bind together, the cell can take glucose (sugar) from the blood and use it for energy [3].

Insulin Regimens

There are a number of different types of insulin that differ in duration of action and time to peak effect. These can be used in various combinations, depending on the needs and goals of the individual patient [1].

All preanalog insulins form hexamers, which must dissociate into monomers subcutaneously before being absorbed into the circulation. Thus, a detectable effect of regular insulin is delayed by 30-60 minutes after injection [4].

Lispro (L) and Aspart (A), insulin analogs, are available, in which altered amino acid position results in more or less rapid absorption. Lispro is a synthetic human insulin analog in which the amino acids at position 28 and 29 (lysine and proline) are reversed. This alteration in insulin structure results in rapid absorption and onset of action [1]. Lispro insulin does not form hexamers (clump of 6 molecules linked together) and is thus faster acting than regular insulin which should be injected 30 minutes or more before meal [3].

The most commonly used regimen in school-aged children involves two subcutaneous injections per day of intermediate acting insulin (NPH or lente, with a duration of about 12-24 hours) and short acting insulin (regular with a duration of about 6-10 hours). This regimen is preferred because it does not require the patient to be given an insulin injection at midday, during school hours.

While Glargine is a new insulin analog in which the amino acid glycine is substituted for asparagine in the A chain of insulin, when insulin Glargine is injected subcutaneously, it precipitates and is thus absorbed very slowly [1].

Injection Sites of Insulin

A person with diabetes injects insulin by putting the needle into the tissue under the skin (subcutaneous tissue).

The places on the body where people can inject insulin most easily are:

- The outer area of upper arm.
- Just above and below the waist, except the area right around the navel (a 2-inch circle).
- The upper area of the buttock, just behind the hip bone.
- The front of the thigh, midway to the outer side, 4 inches below the top of the thigh to 4 inches above the knee.

These areas can vary with the size of the person.

Changing the injection site prevents lumps or small dents from forming in the skin. These lumps or dents are called lipodystrophy. However, people should try to use the same body area for injections that are given at the same time each day, for example, always using the abdomen for the morning injection or an arm for evening injection.

Using the same body area for this routine injection lessens the possibility of changes in the timing and action of insulin [3].

Cutaneous complication of insulin therapy in DM1

1. Lipoatrophy of skin

Common complications of subcutaneous insulin injection include lipoatrophy and lipohypertrophy. Insulin lipoatrophy usually occurs approximately 6 months to 2 years after initiation of relatively high dose of insulin. A dimple or well-circumscribed depression at the site of injection is typically seen, although loss of fat may extend beyond the site of injection, leading to an extensive, depressed plaque. Biopsy reveals a marked decrease or absence of subcutaneous tissue, without inflammation or fibrosis [5]. The development of lipoatrophy may have an immunological basis, predisposed by lipolytic components of certain insulins. Repeated use of the same injection site increases the risk of lipoatrophy. With time, patients learn that these areas are relatively pain free and continue to use them. However, the absorption of insulin from lipoatrophic area is erratic leading to frequent difficulties in achieving ideal blood glucose control. With the increasing use of modified, rapidly absorbed analog insulin (for example, insulin Lispro and insulin Aspart), the incidence of lipoatrophy occurring has decreased over recent years. The likelihood of lipoatrophy can be reduced by regular rotation of injection sites, but once developed, practical benefit may be obtained by insulin injection into the edge of

the area, co-administration of dexamethasone with insulin, or changing the mode of insulin delivery [2].

Lipoatrophy as a cutaneous complication of insulin therapy has been extremely rare since the introduction of recombinant human insulin [6].

Lispro insulin was not reported to be associated with this complication, but recently, a study documented the first two cases of lipoatrophy associated with lispro insulin in two insulin pump-treated patients [7]. Moreover, a singular case was observed, in which lipoatrophy occurred in two different locations with both buffered human regular insulin and lispro insulin in a patient treated by continuous subcutaneous insulin infusion [8].

2. Lipohypertrophy of skin

Bulging of an area of skin (due to fat accumulation) that forms when a person keeps injection insulin into the same spot. Continued injection into these lumpy area delays the absorption of insulin and is not recommended even though injection into lumpy area is painless (as there are no nerve endings in the lumps) [3]. Lipohypertrophy is the most common complication of insulin therapy. Newer insulin has also reduced its prevalence considerably, although its adverse effects on diabetic control is similar to lipoatrophy through impaired absorption of insulin into the systemic circulation. Experience with liposuction at these sites is limited, however, good cosmetic results have been achieved [2].

3. Insulin Allergy

This occurs when a person’s body has an allergic or bad reaction to taking insulin made from pork or beef or from bacteria, or because the insulin is not exactly the same as human insulin or because it has impurities. The allergy can be of two forms. Sometimes an area of skin becomes red and itchy around the place where the insulin is injected. This is called a local allergy.

In another form, a person’s whole body can have a bad reaction, this is called a systemic allergy. The person can have hives or red patches all over the

body or may feel changes in the heart rate and in the rate of breathing. A doctor may treat this allergy by prescribing purified insulin or by desensitization [3].

Allergic reactions to insulin may be immediate or delayed. The immediate local reaction is probably IgE mediated. It starts as erythema, become urticarial within 30 minutes and subsides within an hour. The delayed reaction is the most common reaction. It is due to delayed hypersensitivity. About 2 weeks after the initiation of insulin therapy, a pruritic nodule develops within one to two days at the site of injection, lasts for days and heals with hyperpigmentation and scarring.

Useful adjuncts to managing allergic reactions include addition of dexamethasone to the insulin injection or change in delivery system utilizing insulin pump therapy or potentially inhaled insulin when these become available [2]. A case of human insulin allergy induced by intermediate-acting insulin but not by long-acting insulin has been reported. The patient developed generalized urticaria after injection of intermediate-acting insulin for diabetes mellitus, the patient was then recommended to use long-acting insulin preparation, and became free from symptoms thereafter [9].

4. Edema of skin

Edema of feet and abdomen is a rare phenomenon accompanying initiation of insulin therapy [10], which appears shortly after starting or increasing the dose of insulin. It is commonly seen in women, and is unrelated to cardiac or renal disease. The pathogenesis is unclear [11]. It resolves spontaneously, and successful management with ephedrine has also been described [12].

5. Other cutaneous complications

Localized induration, ulceration and scar formation, cutaneous abscess formation and development of keloid may result from faulty injection techniques. Idiosyncratic reactions are very rare and include pigmentation and occasionally keloid formation. Skin reaction resembling acanthosis nigricans has been reported [12].

Pediatric diabetes education

Unfortunately, most children who meet the hospital's admitting criteria may only have four to five days in the hospital for blood glucose regulation and education [13]. This leaves very little time for the educators to get to know the families and ensure that everyone involved with the child's diabetes control has been properly educated, in addition, some of the patients do not meet the hospital admission criteria, in these instances the insulin regulation and education must be accomplished on an outpatient basis [14].

Diabetes treatment protocol relies heavily on the triad of diet, exercise and insulin, however, many patients fail to see the importance of these responsibilities in their day-to-day life and thus run the risk of complication [15].

Common complications of diabetes mellitus

1. Diabetic ketoacidosis

Is the end of the metabolic abnormalities resulting from a severe deficiency of insulin or insulin effectiveness. The latter occurs during stress as counter regulatory hormones block insulin action. Diabetic ketoacidosis occurs in 20-40% of children with new onset diabetes, and in children with known diabetes who omit insulin doses or who don't successfully manage an intercurrent illness [4]. It may also be caused by stress and psychological problems, and recurrent diabetic ketoacidosis is a particular problem in adolescents and may be fatal [16].

2. Hypoglycemia:

Is the major limitation to tight control of glucose levels. Once injected, insulin absorption and action are independent of the glucose level, thus creating a unique risk of hypoglycemia from an unbalanced insulin effect. Insulin analogs may help reduce but cannot eliminate this risk. Most children with type I diabetes can expect mild hypoglycemia each week, moderate hypoglycemia a few times each year, and severe hypoglycemia every few years. These episodes are usually

not predictable, although exercise, delayed meals or snacks, and wide swings in glucose levels increase the risk [4].

3. Retinopathy

The prevalence of retinopathy in adolescents varies from 18-47%. More than 90% of the patients with type I diabetes will eventually develop some degree of retinopathy. The earliest sign of diabetic eye disease is the development of the background retinopathy which consists of microaneurysms and hemorrhages with exudates which denotes involvement of the macula. This stage is asymptomatic and dos not damage vision. It may stabilize, regress with improved glycogenic control or progress if poor control continues. Background diabetic retinopathy may, rarely in childhood, progress to proliferative retinopathy. This can be successfully treated in its early stages with laser photocoagulation therapy. All patients with retinopathy should be referred to an ophthalmologist. Cataract may affect patients with diabetes but are very rare under the age of 20 years [17].

4. Nephropathy

The cumulative incidence of nephropathy after 40 years of diabetes is at least 40%. Nephropathy may lead to chronic renal failure and necessitate dialysis or renal transplantation. Nephropathy is preceded by the development of persistent microalbuminuria which affects approximately 10% of children and adolescents. Patients with persistent microalbuminuria should have their blood pressure and their serum urea, electrolytes and creatinine concentration measured, and a renal ultrasound should be performed. Attempts should be made to improve glycemic control which may halt the changes. If microalbuminuria persists, treatment with angiotensin-converting enzyme (ACE) inhibitors (e.g. Captopril) should be considered, even in the absence of hypertension. This treatment should not be prescribed until the possibility of nondiabetic renal disease has been excluded [18].

5. Neuropathy

The earliest symptoms include numbness and paraesthesia of the feet or hands with evidence of decreased vibration sense, loss of ankle jerk reflexes and diminution in sensation to pinprick on clinical examination. However, clinically significant neuropathy in adolescence is very rare, although subclinical neuropathy demonstrated by abnormalities of motor nerve conduction velocity have been reported in 20-57% of children with diabetes [17].

6. Growth failure

Chronic ill health conditions such as cystic fibrosis, diabetes mellitus, inflammatory bowel disease, chronic renal failure and asthma could be associated with poor growth and weight gain and a delay in the onset of puberty, although with modern treatment regimens and much more careful attention to nutrition, this is rarely seen [19].

Aims of the Study

1. To determine the prevalence of the various cutaneous complications of insulin therapy in insulin dependent diabetes mellitus (IDDM).
2. To explore the factors that may affect the development of such complications.
3. To assess the implications of having such complications on the general condition of the child.

Patients and Methods

This cross-sectional study recruited 102 patients with type I diabetes mellitus who were attending the outpatient diabetes clinic at Al-Batool Teaching Hospital, Diyala, Iraq, over a period of three months from the first of November, 2022 to the first of February, 2023.

Informed consent was obtained from all individual participants included in the study. A questionnaire form was prepared for collecting the following information:

- Name of the patient.
- Age.
- Sex.
- The person who injects the patient with insulin.
- Academic achievement of the patient, father, mother and any other person who may inject the patient with insulin.
- Date of onset of diabetes.
- Type of insulin used by the patient.
- Sites of insulin injection and whether these are changed occasionally, frequently, or not at all.
- Has the patient received any education about the usual sites and techniques of insulin injection? If so by whom?
- Presence of any cutaneous complications (lipohypertrophy, lipoatrophy, allergy and others), on examination.
- Is insulin being injected using the correct technique? Checking the technique first-hand when possible.
- Has the patient with cutaneous complications received any new instructions about the technique and site of the insulin injection?
- Any family history of IDDM in close relatives?

Results

The total number of patients enrolled in the current study was 102 patients, of whom 44 (43.1%) were males and 58 (56.9%) were females, with a male to female ratio of 1:1.3, as demonstrated in Figure 1.

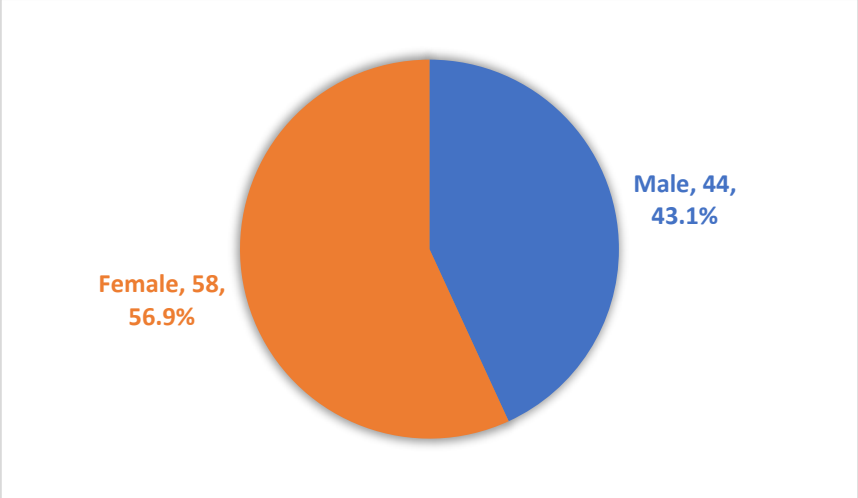

Figure 1: Distribution of the patients according to sex.

34 patients (33%) were below the age of 5 years, 56 patients (55%) were 5 to less than 10 years old, and 12 patients (12%) were 10 to less than 15 years of age, as illustrated in Figure 2.

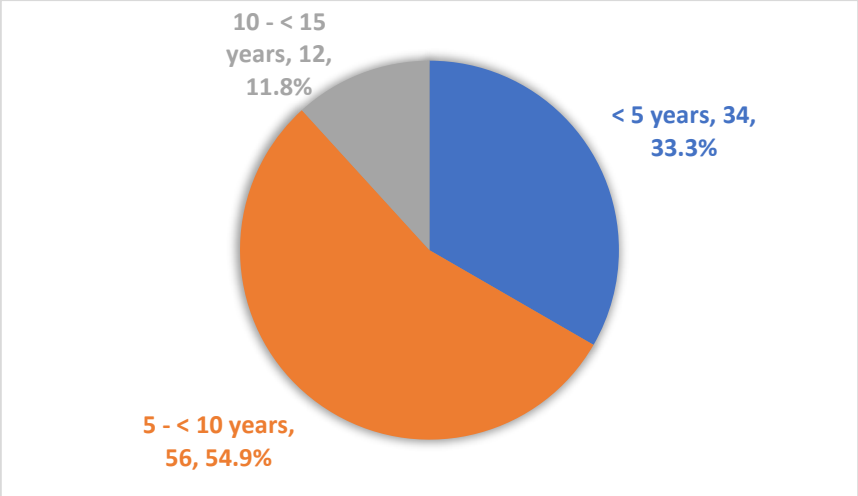

Figure 2: Distribution of the patients according to age.

The cutaneous complications of insulin therapy were present in 57 (55.9%) patients and absent in the remaining 45 (44.1%) patients, as shown in Figure 3.

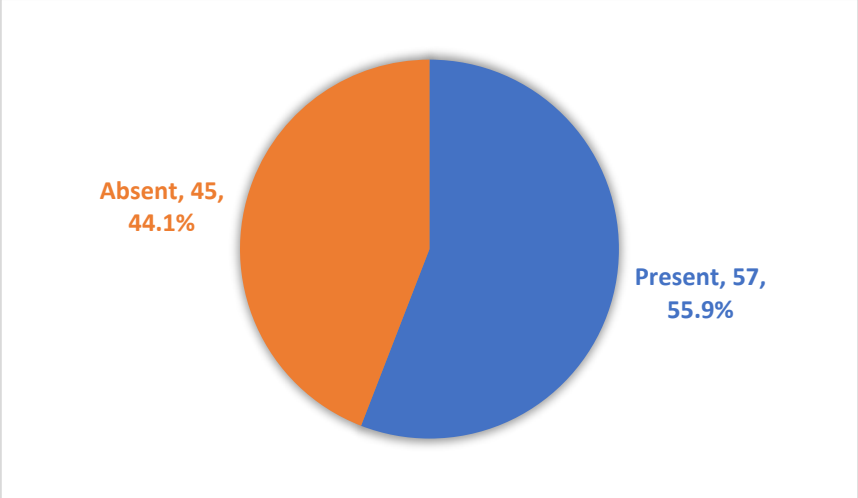

Figure 3: Distribution of patients according to the presence of cutaneous complications of insulin therapy.

Seventy-three (71.6%) patients had diabetes for less than 5 years, 36 (49.3%) of them had cutaneous complications and 37 (50.7%) had no cutaneous complications. Twenty (19.6%) patients had diabetes for 5-10 years, 13 (65%) of them had cutaneous complications while 7 (35%) had no complications.

Nine (8.8%) patients had diabetes for more than 10 years, 8 (88.9) of them had cutaneous complications while only 1 (11.1%) had no complications, as seen in Table 1.

Table 1: Distribution of patients according to the duration of diabetes mellitus.

Duration of diabetes in years	Patients with cutaneous complications No. (%)	Patients without cutaneous complications No. (%)	Total No. (%)
< 5	36 (49.3%)	37 (50.7%)	73 (71.6%)
5-10	13 (65%)	7 (35%)	20 (19.6%)
> 10	8 (88.9%)	1 (11.1%)	9 (8.8%)
Total	57 (55.9%)	45 (44.1%)	102 (100%)

Figure 4 shows that, out of 57 patients with cutaneous complications of insulin therapy, lipohypertrophy was present in 53 (93%) patients and allergy in 4 (7%) patients, while lipoatrophy and other complications were not reported.

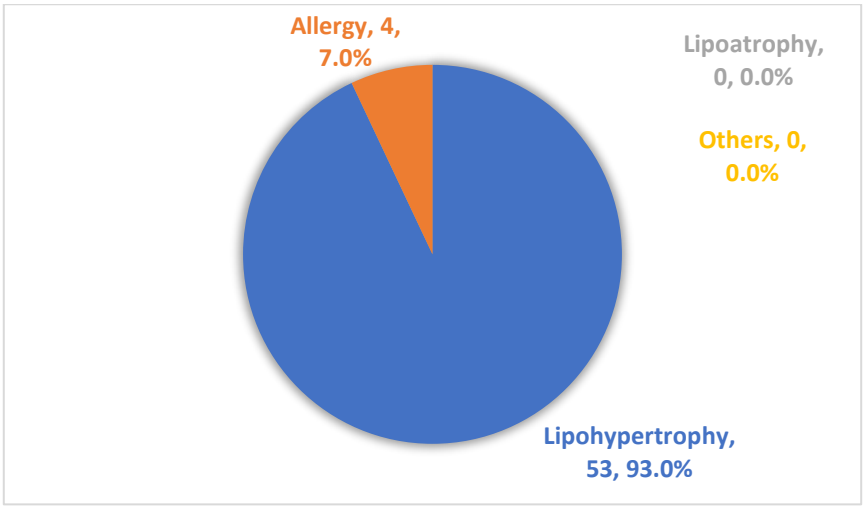

Figure 4: Distribution of patients according to the type of cutaneous complications.

Figure 5 reveals that, among 102 patients, 39 (68.4%) had right and left arm lipohypertrophy and allergy, 5 (8.8%) had right and left thigh lipohypertrophy, 3 (5.3%) had right and left arm and thigh lipohypertrophy, 5 (8.8%) had right arm lipohypertrophy only, 3 (5.3%) had left arm lipohypertrophy only and two patients had complications at unusual sites of insulin injection, one (1.7%) had leg lipohypertrophy while the other (1.7%) had forearm lipohypertrophy.

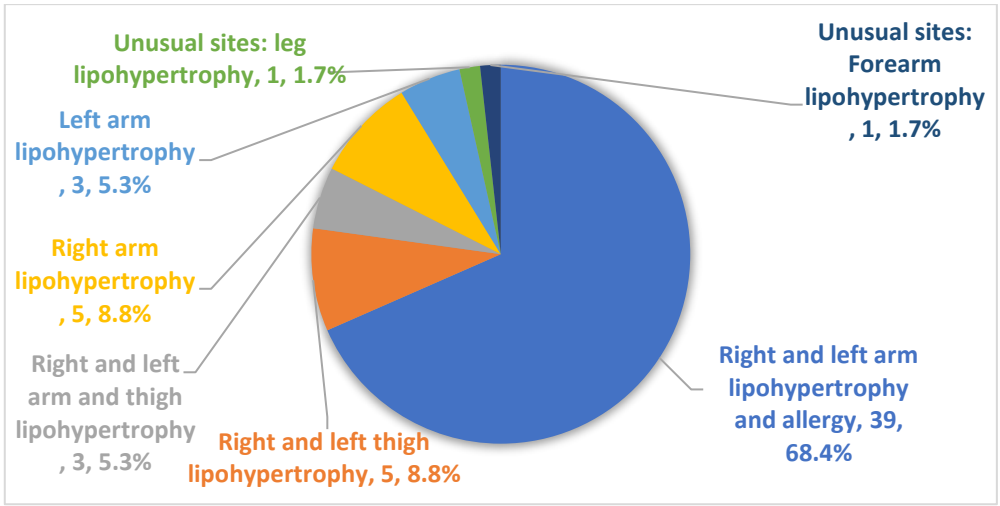

Figure 5: Distribution of patients with cutaneous complications according to the site of insulin injection.

Table 2 displays that, among 102 patients, 15 (14.7%) patients had repeated attacks of diabetic ketoacidosis, 10 (9.9%) of them had cutaneous complications and 5 (4.92%) had no cutaneous complications.

Three (2.9%) patients had hypoglycemia, all of them had cutaneous complications.

Sixteen (15.7%) patients had retinopathy, 13 (12.7%) of them had cutaneous complications and 3 (2.94%) had no cutaneous complications.

Nine (8.9%) patients had nephropathy, 7 (6.9%) of them had cutaneous complications and 2 (1.96%) had no cutaneous complications.

Five (4.9%) patients had neuropathy, 4 (3.9%) of them had cutaneous complications and 1 (0.98%) patient had no cutaneous complications.

Three (2.9%) patients had growth failure, all of them had cutaneous complications.

So, from 57 (55.9%) patients with cutaneous complications, 40 (70.2%) patients had other complications of diabetes and 17 (29.8%) had no other complications. On the other hand, among 45 (44.1%) patients with no cutaneous complications, 11 (24.4%) patients had other complications and 34 (75.6%) patients had no other complications of diabetes.

Table 2: Distribution of the patients according to the common complications of diabetes mellitus.

Common complications of D.M.	Patients with cutaneous complications No. (%)	Patients without cutaneous complications No. (%)	Total No. (%)
Diabetic ketoacidosis	10 (9.8%)	5 (4.9%)	15 (14.7%)
Hypoglycemia	3 (2.9%)	0 (0%)	3 (2.9%)
Retinopathy	13 (12.7%)	3 (3%)	16 (15.7%)
Nephropathy	7 (6.9%)	2 (2%)	9 (8.9%)
Neuropathy	4 (3.9%)	1 (1%)	5 (4.9%)
Growth failure	3 (2.9%)	0 (0%)	3 (2.9%)
No complications	17 (16.7%)	34 (33.3%)	51 (50%)
Total	57 (55.9%)	45 (44.1%)	102 (100%)

Eight (7.8%) patients injected insulin in one site, all of them had cutaneous complications. Fifty (49%) patients change the injection site occasionally, 45 (90%) of them had complications and 5 (10%) of them had no complications, while 44 (43.2%) patients change the site frequently, only 4 (9.1%) of them had complications and 40 (90.9%) of them had no complications, as explained in Table 3.

Table 3: Distribution of patients according to the frequency of changing insulin injection site.

Frequency of changing insulin injection site	Patients with cutaneous complications No. (%)	Patients without cutaneous complications No. (%)	Total No. (%)
No changing	8 (100%)	0 (0%)	8 (7.8%)
Occasionally	45 (90%)	5 (10%)	50 (49%)
Frequently	4 (9.1%)	40 (90.9%)	44 (43.2%)
Total	57	45	102 (100%)

Eighty-four (84.4%) patients use both Actrapid and Monotard insulin, 44 (52.4%) of them had cutaneous complications and 40 (41.6%) had no complications, while 18 (17.6%) patients use Mixtard insulin, 13 (72.2%) of them had complications and 5 (17.8%) had no complications, as exhibited in Table 4.

Table 4: Distribution of patients according to the type of insulin used.

Type of insulin used	Patients with cutaneous complications No. (%)	Patients without cutaneous complications No. (%)	Total No. (%)
Actrapid and Monotard	44 (52.4%)	40 (41.6%)	84 (82.4%)
Mixtard	13 (72.2%)	5 (27.8%)	18 (17.6%)
Total	57	45	102 (100%)

Ninety-seven (95.1%) patients use right technique for insulin injection, 52 (53.6%) had cutaneous complication and 45 (46.4%) had no complications, while

5 (4.9%) patients use wrong injection technique, all of them (100%) had complications, as established in Table 5.

Table 5: Distribution of patients according to the technique of insulin injection.

Technique of insulin injection	Patients with cutaneous complications No. (%)	Patients without cutaneous complication No. (%)	Total No. (%)
Right way	52 (53.6%)	45 (46.4%)	97 (95.1%)
Wrong way	5 (100%)	0 (0%)	5 (4.9%)
Total	57	45	102 (100%)

Regarding the academic achievement of the person who injects the insulin, 12 (11.8%) were illiterate, 28 (72.5%) finished primary school, 43 (42.1%) finished secondary school and 19 (18.6%) finished institute or college. In all these groups, there is no much difference between those with and without cutaneous complications, as described in Table 6.

Table 6: Distribution of patients according to the academic achievement of the person who injects the insulin.

Academic achievement	Patients with cutaneous complications. No. (%)	Patients without cutaneous complications No. (%)	Total No. (%)
Illiterate	7 (58.3%)	5 (41.7%)	12 (11.8%)
Primary school	14 (50%)	14 (50%)	28 (27.5%)
Secondary school	26 (60.5%)	17 (39.5%)	43 (42.1%)
Institute or college	10 (52.6%)	9 (47.4%)	19 (18.6%)
Total	57	45	102 (100%)

Table 7 demonstrates that only 14 (13.7%) patients had a positive family history of IDDM in close relatives, 6 (42.9%) of them had cutaneous complications and 8 (57.1%) had no complications.

Table 7: Distribution of patients according to family history of IDDM.

Family history of IDDM	Patients with cutaneous complications No. (%)	Patients without cutaneous complications No. (%)	Total No. (%)
Positive	6 (42.9%)	8 (57.1%)	14 (13.7%)
Negative	51 (58%)	37 (42%)	88 (86.3%)
Total	57	45	102 (100%)

Discussion

In this study it is apparent that the number of patients with cutaneous complications is more than those without complications, this finding may be related to either poor education of the families and patients or failure of them to follow the instructions given during education and follow up properly.

Lipohypertrophy is the most common complication seen in the current study and this finding is consistent with the findings of similar previous studies. This is probably due to poor education or the desire of the patient to inject insulin into the lumpy areas to avoid pain [2].

Lipoatrophy was not reported, as it is rare since the introduction of recombinant human insulin [6], and patients in the current study use human insulin.

The incidence of these cutaneous complications is high during the early years of treatment and increases with time as its development does not require much time and most patients fade up from continuous following of the instructions given during education.

Majority of patients in this study use the upper arm for insulin injection and when lipohypertrophy occurs they continue to inject in the same area as it becomes painless as there are no nerve endings in the lump [3].

The current study reported two cases of insulin injection in unusual sites with complications, leg lipohypertrophy and forearm lipohypertrophy which happened because of wrong information given to the patients about the different sites of insulin injection or because they did not follow the instructions correctly.

In the current study, 70.2% of patients with cutaneous complications had other complications of diabetes, while 75.6% of those without cutaneous complications had no other complications of diabetes, which could be explained on basis of poor education and management in the first group, in addition to the fact that lipohypertrophy impairs proper absorption from the site of insulin injection [2], which may affect the control of blood sugar, so patients develop

different types of complications, whereas those with good education and management had a lower incidence of complications.

In this study, lipohypertrophy developed in 100% of patients who inject the insulin in one area (without changing), and in 90% of those who only change the injection site occasionally, and this may be related to poor education or because the site of lipohypertrophy becomes painless and other sites remain relatively painful.

The current study revealed that there is no much difference in the incidence of developing cutaneous complications based on the type of insulin used, except in those who use Mixtard insulin, and this can be explained by the fact that the majority patients enrolled in the current study use a combination of Actrapid and Monotard, and the minority use Mixtard because it is not always available for them, and it is usually reserved for those family with poor education, so the higher incidence of cutaneous complications may also be related to this cause.

All patients in the current study, who used wrong technique of insulin injection developed cutaneous complication. This can be due to poor education regarding the injection technique, however, many other patients who used right technique, also had complications, and this may be related to other factors.

The academic achievement of person who injects the insulin, in this study, had no role in decreasing the incidence of developing cutaneous complications and this leads us to the conclusion that this depends mainly on education given in the diabetes wards and clinics by the doctors and medical staff. It also depends on whether or not the patients follow the instructions about injection site and technique that were given during the education, and those who did not follow the instructions (84.4%) developed cutaneous complications.

It was rational to think that the presence of family history of IDDM in close relative would have a beneficial effect in decreasing the incidence of this type of complications, but it seems that it had no effect, as far as the current study is

concerned, as some of these family members may actually contribute to the patient adopting bad and wrong practices.

Conclusions and Recommendations

Conclusions

1. Lipohypertrophy is the most common complication of insulin therapy in IDDM.
2. Cutaneous complications occur during the first few years after initiation of insulin therapy and their incidence increases over time.
3. The most common sites of insulin injection in the body used by the patients and the sites of occurrence of cutaneous complications are the upper arms of the patients.
4. Cutaneous complications are associated with an increase in the incidence of other complications of diabetes.
5. The most important cause of developing cutaneous complications is poor educations about insulin injection site and technique, or failure of the patients to follow the instructions given during education, as the academic achievement of the person who injects the insulin has no role.

Recommendations

1. Focus needs to be given to proper education of the family and the patients, and instructions about the insulin injection site and technique need to be made readily available for the family and the patients.
2. Rotation of the insulin injection sites, at the usual sites, needs to be done at regular intervals.
3. Examination of the insulin injection sites needs to be undertaken at each visit to the diabetes clinic to avoid the development of cutaneous complications.
4. The technique of insulin injection should be checked periodically especially in patients who start developing cutaneous complications or when the person who injects the insulin changes.
5. Any diabetic patient with cutaneous complications needs to be examined for the presence of other more serious complications.

References

1. Marcdante KJ, Kliegman RM, Schuh AM. Nelson Essentials of Pediatrics. 9th ed. Philadelphia, PA, USA: Elsevier; 2022.
2. Yanachkova V, Staynova R. Insulin-induced Lipoatrophy in a Patient on Insulin Analogue Therapy: a Case Report. Folia Med (Plovdiv). 2020;62(3):597-600. doi:10.3897/folmed.62.e50166
3. Diabetes India (2022). Diabetes Dictionary [online]. Website http://diabetesindia.com/diabetes-causes-preventions/more/dictionary.html [accessed 17, February, 2023].
4. Binder E, Lange O, Edlinger M, et al. Frequency of dermatological side effects of continuous subcutaneous insulin infusion in children and adolescents with type 1 diabetes. Exp Clin Endocrinol Diabetes. 2015;123(4):260-264. doi:10.1055/s-0034-1394381
5. Conwell LS, Pope E, Artiles AM, Mohanta A, Daneman A, Daneman D. Dermatological complications of continuous subcutaneous insulin infusion in children and adolescents. J Pediatr. 2008;152(5):622-628. doi:10.1016/j.jpeds.2007.10.006
6. Griffin ME, Feder A, Tamborlane WV. Lipoatrophy associated with lispro insulin in insulin pump therapy: an old complication, a new cause?. Diabetes Care. 2001;24(1):174. doi:10.2337/diacare.24.1.174
7. Holstein A, Stege H, Kovacs P. Lipoatrophy associated with the use of insulin analogues: a new case associated with the use of insulin glargine and review of the literature. Expert Opin Drug Saf. 2010;9(2):225-231. doi:10.1517/14740330903496402
8. Fineberg NS, Fineberg SE, Anderson JH, Birkett MA, Gibson RG, Hufferd S. Immunologic effects of insulin lispro [Lys (B28), Pro (B29) human insulin] in IDDM and NIDDM patients previously treated with insulin. Diabetes. 1996;45(12):1750-1754. doi:10.2337/diab.45.12.1750
9. Hasselmann C, Pecquet C, Bismuth E, et al. Continuous subcutaneous insulin infusion allows tolerance induction and diabetes treatment in a type

1 diabetic child with insulin allergy. Diabetes Metab. 2013;39(2):174-177. doi:10.1016/j.diabet.2012.10.002

10. Ji LN, Wu S, Fu DQ, et al. Jieduquyuziyin Prescription alleviates hepatic gluconeogenesis via PI3K/Akt/PGC-1α pathway in glucocorticoid-induced MRL/lpr mice. J Ethnopharmacol. 2022;284:114815. doi:10.1016/j.jep.2021.114815
11. Fullerton B, Jeitler K, Seitz M, Horvath K, Berghold A, Siebenhofer A. Intensive glucose control versus conventional glucose control for type 1 diabetes mellitus. Cochrane Database Syst Rev. 2014;2014(2):CD009122. doi:10.1002/14651858.CD009122.pub2
12. The Diabetes Control and Complication Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complication in insulin-dependent diabetes mellitus. N Engl J Med. 1993;329:977-986.
13. Berg AK, Nørgaard K, Thyssen JP, et al. Skin Problems Associated with Insulin Pumps and Sensors in Adults with Type 1 Diabetes: A Cross-Sectional Study. Diabetes Technol Ther. 2018;20(7):475-482. doi:10.1089/dia.2018.0088
14. Reichard P, Nilsson BY, Rosenqvist U. The effect of long-term intensified insulin treatment on the development of microvascular complications of diabetes mellitus. N Engl J Med. 1993;329(5):304-309. doi:10.1056/NEJM199307293290502
15. Wang PH, Lau J, Chalmers TC. Meta-analysis of effects of intensive blood-glucose control on late complications of type I diabetes. Lancet. 1993;341(8856):1306-1309. doi:10.1016/0140-6736(93)90816-y
16. Castellanos L, Tuffaha M, Koren D, Levitsky LL. Management of Diabetic Ketoacidosis in Children and Adolescents with Type 1 Diabetes Mellitus. Paediatr Drugs. 2020;22(4):357-367. doi:10.1007/s40272-020-00397-0

17. Subramanian S, Baidal D. The Management of Type 1 Diabetes. In: Feingold KR, Anawalt B, Blackman MR, et al., eds. Endotext. South Dartmouth (MA): MDText.com, Inc.; May 22, 2021.
18. Cobeñas CJ, Spizzirri FD. Microalbuminuria in insulin-dependent diabetes mellitus always indicative of diabetic nephropathy?. Pediatr Nephrol. 2003;18(3):309-310. doi:10.1007/s00467-002-1016-x
19. Krysiak R, Rudzki H, Okopień B. Cukrzyca i stany przedcukrzycowe w chorobach gruczołów wydzielania wewnetrznego [Diabetes and prediabetes in endocrine disorders]. Wiad Lek. 2012;65(3):187-198.

بسم الله الرحمن الرحيم

جمهورية العراق

وزارة التعليم العالي و البحث العلمي

جامعة ديالى - كلية الطب

المضاعفات الجلدية للعلاج بالانسولين في الاطفال المصابين بداء السكري من النوع ١ في مستشفى البتول التعليمي

بحث تخرج مقدم الى كلية الطب - جامعة ديالى

كجزء من متطلبات نيل درجة البكالوريوس في الطب والجراحة العامة

من قبل

سلمان مهدي سلمان

بإشراف

الدكتور

محمد قاسم صالح

بكالوريوس طب وجراحة عامة، ماجستير احياء مجهرية طبية

فرع طب الاسرة والمجتمع

كلية الطب - جامعة ديالى

٢٠٢٢-٢٠٢٣

الخلاصة

يتميز داء السكري بارتفاع السكر في الدم والسكر في البول ويحدث كنقطة نهاية مشتركة للعديد من العمليات المرضية. النوع الأكثر شيوعًا الذي يحدث في الطفولة هو النوع الأول من داء السكري (DM1) ، والذي ينتج عن تدمير المناعة الذاتية للبنكرياس. يعاني مرضى DM1 من نقص حاد و دائم في الأنسولين ويحتاجون إلى الأنسولين للبقاء على قيد الحياة والوقاية من نوبات الحماض الكيتوني التي تهدد الحياة.

تشمل المضاعفات الجلدية للعلاج بالأنسولين الضخم الشحمي والضمور الشحمي والحساسية وغيرها.

الهدف من الدراسة هو:

١. لتحديد مدى انتشار المضاعفات الجلدية المختلفة للعلاج بالأنسولين في داء السكري المعتمد على الأنسولين.

٢. استكشاف العوامل التي قد تؤثر على تطور مثل هذه المضاعفات.

٣. تقييم انعكاسات حدوث مثل هذه المضاعفات على الحالة العامة للطفل.

خلال الفترة من الأول من نوفمبر وحتى الأول من فبراير ٢٠٢٢-٢٠٢٣ ، تم تقييم مرضى السكري من النوع الأول الذين يحضرون إلى عيادة مرضى السكري في مستشفى البتول التعليمي للأطفال من أجل المضاعفات الجلدية للعلاج بالأنسولين في مواقع الحقن.

بلغ العدد الإجمالي للعينة ١٠٢ مريض بنسبة ذكور إلى إناث ١:١,٣.

تحدث المضاعفات الجلدية في ٥٥,٩٪ منهم وكانت أكثر المضاعفات الجلدية شيوعًا للعلاج بالأنسولين في مرض السكري المعتمد على الأنسولين هي تضخم الجلد الدهني (٩٣٪) ، وتحدث الحساسية تجاه الأنسولين في ٧٪ بينما لم يتم الإبلاغ عن الضمور الشحمي والمضاعفات الجلدية الأخرى .

ترتبط المضاعفات الجلدية بزيادة حدوث مضاعفات أخرى لمرض السكري.

تحدث معظم هذه المضاعفات في أعلى الذراعين لأنها الأماكن المعتادة التي يستخدمها المرضى لحقن الأنسولين وخاصة في أولئك الذين إما لم يغيروا المواقع أو يغيروها من حين لآخر وأيضًا أولئك الذين لديهم تقنية خاطئة للحقن، كل هذه إما بسبب ضعف التعليم أو عدم اتباع التعليمات ، حيث لا دور للتحصيل الدراسي للشخص الذي يحقن الأنسولين للمريض.

لذا ، فإن التثقيف المناسب حول مواقع وتقنية حقن الأنسولين والحفاظ على هذا التثقيف هو العامل الأساسي في منع تطور هذه المضاعفات.