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Original Article

Lipohypertrophy in Individuals with Type 2 Diabetes: Prevalence and Risk Factors

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ABSTRACT

Introduction: As well as its negative effect on the subcutaneous tissues, lipohypertrophy has negative effects on clinical data. The purpose of this study was to examine the frequency of lipohypertrophy, risk factors and perceived barriers preventing rotation in individuals with type 2 diabetes.

Methods: This descriptive cross-sectional study was conducted at Diabetes Education Center and Endocrine and Metabolism Clinic of a university hospital and Diabetes Education and Monitoring Center in a private hospital in Turkey between June 2016- April 2017. The inclusion criteria were as follows; undergoing at least one year of insulin therapy, injecting insulin pens or syringes themselves, being over 18 years of age, making regular injection of insulin and being a patient with type 2 diabetes. Introductory information form was used to collect the data. The data were analyzed using descriptive statistics and chi-square analysis with SPSS version 16.0.

Results: Factors influencing lipohypertrophy development were determined as follows; healthcare personnel who provide insulin education, duration of diabetes, the number of injection administered daily, needle length, the number of injection sites, insulin types, injection site rotation and intra-site rotation and needle exchange frequency. In addition, the prevalence of lipohypertrophy was found to be higher in patients with hypoglycemia, unexplained hypoglycemia, and those with high BMI and A1C.

Conclusion: It is recommended that diabetes education should be provided by the diabetes specialist nurses who have diabetes-specific certifications and / or education and who can provide full-time education. Randomized controlled interventional studies investigating how to prevent the lipohypertrophy development are also needed.

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Introduction

Lipodystrophy is the becoming of the tissue as 'rubber-like texture' by thickening and swelling. It may be sometimes soft and sometimes hard. Although lipodystrophy is more common in type 1 diabetes, its frequency is considerably high in type 2 diabetes.[1-4] In the literature, the prevalence of lipohypertrophy was reported to be 37.3% in patients with type 2 diabetes in Saudi Arabia;[1] 48.8% in patients with type 1 and type 2 diabetes in Turkey;[3] 64.4% in type 1 and type 2 patients in Spain,[2] and 35.26% in China.[4]

Factors influencing the development of lipodystrophy were reported as follows; the duration of insulin therapy, daily insulin dose, the number of injections per day, gender, body mass index (BMI), injection site, not rotating the injection site, using a pen or syringe, needle length and the frequency of needle exchange, insulin type[5] and poor glycemic control.[1,2,3,6]

As well as its negative effect on the subcutaneous tissues, lipohypertrophy has negative effects on clinical data.[2,7-9] The pain sensation is reduced in the injection site where lipohypertrophy develops, and individuals with diabetes may be willing to inject at this site continuously because of not having a sense of pain. While the whole insulin dose injected at healthy/normal subcutaneous tissue is absorbed, hypoglycemia risk can be experienced in the lipohypertrophic region due to impaired absorption of insulin.[2,7-9]

In a study conducted in Spain, it was found that 49.1% of individuals with diabetes and lipohypertrophy have severe unknown hypoglycemia whereas this ratio was 5.9-6.5% in individuals with diabetes and without LH.[2] It was determined in a study conducted in Spain that although 49.1% of the individuals with diabetes and lipohipthophy experience unexplained severe hypoglycemia, this ratio was only 5.9-6.5% in individuals with diabetes and without lipohipthophy.[2]

Because of problems in absorption of insulin and decreased sense of pain, patients mostly prefer lipohypertrophic region for insulin injection and this causes an increase in insulin consumption and thus in costs.[2] In literature review, there is no research examining patients' perceptions regarding the reasons for lack of site rotation, which is important for the development of lipohypertrophy. In addition, there is no other research conducted to examine the relationship between lipohypertrophy and the number of areas used by patients for insulin injection or to investigate the influence of the diabetes educator giving insulin education on the development of lipohypertrophy. From this point of view, this study is important because of the fact that it involves a large sample group and investigates the perceived barriers preventing site rotation in individuals with diabetes. In addition, it is a study examining that how technological devices (such as needle size and pen) affect the

prevalenceof lipohipertrophy in a region of Turkey over a ten-year of period. It is thought that the findings obtained will guide diabetes educators both in clinical and patient education. In this study, the purpose was to examine the frequency of lipohypertrophy, risk factors and perceived barriers preventing rotation of injection site in individuals with type 2 diabetes.

Materials and methods

This descriptive cross-sectional study was conducted at Diabetes Education Center and Endocrine and Metabolism Clinic of a university hospital and Diabetes Education and Monitoring Center in a private hospital in Turkey between June 2016 and April 2017. The inclusion criteria were as follows; undergoing at least one year of insulin therapy, injecting insulin pens or syringes themselves, being over 18 years of age, making regular injection of insulin and being a type 2 individual with diabetes. Patients not using insulin and / or using insulin therapy temporarily, patients unable to use any site of injection due to mastectomy or any other reasons, patients with medical instability, visual, audition and movement problems, psychiatric patients who cannot administer insulin injection, patients receiving transient insulin treatment. Women with gestational diabetes and decompensate patients who do not normally use insulin, but develop acute hyperglycemia and those hospitalized and using insulin pumps were excluded from the study. The sample of the study consisted of 436 type 2 individuals with diabetes.

In this study, power analyses were performed using G*Power software version 3.1.[10] At the end of the study, the effect size was 0.5 (P=0.05), and according to the post hoc, x^2 tests analysis was conducted for 436 patients, and the power of the study was calculated as 0.99.

To collect the data, "Introductory information form" developed in accordance with the literature, was used.[1-3,6]

Introductory information form includes questions regarding socio-demographic and diabetic patterns of the patients. The content of the form involves age, gender, education status, duration of diabetes diagnosis, healthcare personnel providing insulin education, type and duration of insulin treatment, devices used for injection, the number of daily injections, total insulin dose administered daily, needle length, injection sites, needle reuse frequency, intra-site rotation or injection site rotation, lipohypertrophy presence and location, BMI, A1C, hypoglycemia and unexplained hypoglycemia. The information regarding age, gender, educational status of the patients, health personnel who provides insulin education, injection sites, duration of insulin therapy, devices used at home, re-use, frequency / status of the needles, rotation/rotation site, hypoglycemia and unexplained hypoglycemia were obtained from the patients' own statements. Other data such as the type of insulin treatment, the number of daily injections, the daily injected insulin dose, the needle length and BMI and the A1C values of the patient for the last three months were obtained from the medical records. The presence and location of lipohypertrophy was assessed by certified diabetes nurses using inspiration and palpation method.

Clinical guidelines recommend the systematic switching of insulin injections from one site to another.[11] Proper site rotation is defined as the use of a new injection site at each injection of insulin in a systematic manner. The most common and effective scheme is to divide quadrants or halves (thighs, buttocks and arms) and switch to each piece to the other part clockwise after one week of use.[11]

Rotating between injection sites: The term of site rotation in this study defines the patients who use different sites at insulin injection on each day, for every 2-5 days or for each injection.[11]

Rotating within injection sites: Defined as a distance of at least 1 cm between injections (at least 1 cm apart).[11]

Hypoglycemia: Defined as presence of one or more symptoms associated with hypoglycemia (palpitations, fatigue, sweating, hunger, dizziness and tremor) and confirmation of blood glucose level of ≤ 60 mg/ dl on blood glucose meter.[2]

Unexplained recurrent hypoglycemia: Defined as the development of hypoglycemic episodes at least once or more than one in a week without an identifiable triggering event, such as drug treatment, dietary or activity changes.[2]

Lipohypertrophy: Lipohypertrophy evaluation requires both inspection and palpation examination of the injection sites. For this reason, the health care worker should first evaluate the injection site visually, then mass status in the swollen site with the thumb and forefinger.[2,6] The mass is specified as "present" or "not present".

Data were collected by two certified diabetes nurses (educators). After giving information to the individuals with diabetes about the study, the data were collected from the patients who agreed to participate in the study through face-to-face interviews. For the evaluation of lipohypertrophy, data were collected via inspection and palpation. A total of 445 patients were reached during the data collection process but 9 patients (2 had type 1 diabetes, 2 had lipoatrophy, 3 underwent mastectomy and 2 had scar tissue in the limbs) were excluded from the study. As a result, 436 patients were included in the data analysis section of the study. In the study, the mean duration of data collection was 15 min.

Ethical approval for the study was obtained from the ethics committee of University Medical Faculty Non-Interventional Clinical Investigations (Number: 233, date: 02.06.2016). After determining the individuals who meet the inclusion criteria, the patients were informed about the study and informed consent form was obtained from all patients with diabetes who agreed to participate in the study.

For the statistical analyzes, SPSS 16.0 (Statistical Package for Social Sciences) program was used. After loading the data, the missing or incorrect data entry was evaluated and the data were verified. For descriptive information of the individuals with diabetes, numbers and percentages, descriptive statistics, were used. Chi-square analysis was performed to assess the factors affecting the lipohypertrophy development in individuals with diabetes, $P<0.05$ was considered significant.

Results

Socio-demographic characteristics of the individuals with diabetes constituting the sample group revealed that 63.5% of the patients were female and 36.5% were male; 37.6% were at the age of 60-69 years, 34.4% were primary school graduates, 48.1% were overweight, and 62.8% previously received insulin education from nurses (Table 1).

Considering the characteristics associated with diabetes, the duration of diabetes was ≥ 10 years in % 65.6 of the patients with diabetes, 57.8% received diabetes treatment between 3-9 years, 32.6% had two injections daily, 34.6% used 5 mm-needles, 41.5% used the three sites for insulin injection, 59.6 received daily dose of insulin less than 50% units, 41.1% administered pre-mixed insulin's and 63.5% had no systematic rotation. In addition, the ratio of the patients who do not change needle tip for each injection was 63.8%. Of the patients, 44.0% had hypoglycemia and 24.3% had unexplained hypoglycemia. In 49.0% of the individuals, A1C level was 9 or above and 43.8% experienced lipohypertrophy (Table 1). Lipohypertrophy was mostly observed in arms (41.7%) and followed by abdomen (35.7%) (Figure 1). Besides, the ratio of lipohypertrophy was found to be %22 in the thigh, yet no lipohypertrophy was found in buttocks (Figure 1).

The reasons preventing the rotation were as follows; twenty-seven percent of the individuals with type 2 diabetes were found to have arm or leg pain and / or bleeding after insulin injection, 25.1% had physical difficulty in gripping the arm or taking off clothes from their legs, 24.0% reported fattening in the abdomen after insulin usage (Table 2), 20.0% reported that injection through abdomen or arm was much more practical, 3.0% was afraid of injecting into the abdomen or arm, and 0.9% prefer abdominal injection due to the wider application area (Table 2).

The difference between the prevalence of lipohypertrophy with respect to gender, age, educational status, the duration of insulin treatment and the amount of daily insulin was not statistically significant (P> 0.05) (Table 3). Lipohypertrophy was significantly more come in patients having a duration of diabetes ≥10 years than those with a duration of less than 10 years (P = 0.003) (Table 3).

Considering the insulin injection technique, lipohypertrophy was found to be more common in patients who received "education on insulin administration technique" from the doctor (65.8%, P<0.001), and those having four injections per day (54.1%, P = 0.014) and using only one site for insulin injection (80.7%, P <0.001) (Table 3).

Analysis of the needle length and type of insulin used in individuals with type 2 diabetes revealed that the likelihood of lipohypertrophy was significantly lower in patients using 5 mm needle (31.1%; P <0.001) and those administering only basal insulin (34.6%; P=0.037) (Table 3). In addition, the prevalence of lipohypertrophy was statistically significantly higher in patients who failed to systematically alternate the injection site (48.2%; P <0.001) and in individuals not performing intra-site rotation (63.5%, P <0.001) and patients preferring recurrent needle use (69.2%; P = 0.014) (Table 3).

Table 1. Introductory features of individuals with type 2 diabetes

Variable	N (%)*N=436
Gender	
Female	277 (63.5)
Male	159 (36.5)
Age (year)	
<50	48(11.0)
50-59	111(25.5)
60-69	164(37.6)
≥70	113(25.9)
Educational status	
Non-literate	33(7.6)
Primary school graduate	150(34.4)
Secondary School graduate	118(27.1)
High School or University graduate	135(31.0)
BMI kg/m^2	
Normal weight	74(17.0)
Over weight	210(48.1)
Obese	152(34.9)
Training provider	
Nurse	274(62.8)
Doctor	120 (27.5)
Chemist	42(9.7)
The duration of diabetes diagnosis	
1-10 year	150(34.4)
≥10	286(65.6)
The duration of diabetes therapy (year)	
≤2	73(16.7)
3-9	252(57.8)
≥10	111(25.5)
The number of daily injection	
1	128 (29.5)
2	142 (32.6)
3	55(12.6)
4	111(25.5)
Needle length	
4 mm	133(30.5)
5 mm	151(34.6)
6 mm	117(26.8)
8 mm	35(8.0)
Injection site	
Single site (Abdomen, arms or legs)	88(20.2)
Two sites (Abdomen and arms or abdomen or legs)	167(38.3)
Three sites (Abdomen, arms, legs, or arm, leg and hip)	181(41.5)
The amount of insulin administered daily	
≤50 unit/day	260(59.6)
>50 unit/day	176(40.4)
Types of insulin	
Only basal	133(30.5)
Basal + Bolus	124(28.4)
Pre-mixed insulin's	179(41.1)
Between sites rotation	
Performing Systematic rotation	277(63.5)
Not performing Systematic rotation	159(36.4)
Intra-sites rotation (At least 1 cm distance between inject-ions)	
Yes	291(66.7)
No	145(33.3)
The frequency of needle change	
At each injection	158(36.2)
Not at each injection (at least 3-time use)	278(63.8)
Hypoglycemia	
Yes	192(44.0)
No	244(56.0)
Unexplained recurrent hypoglycemia	
Yes	106(24.3)
No	330(75.7)
A1C	
<7	65(14.9)
7-7.9	53(12.2)
8-8.9	104(23.9)
≥9	214(49.0)
Lipohypertrophy	
Present	191(43.8)
Not present	245(56.2)

*All patients use insulin pen.

With respect to clinical findings, advanced statistical analysis results revealed that the prevalence of lipohypertrophy was significantly higher in obese category (47.5%; P= 0.009) and in patients with A1C level of ≥ 9 (68.7%, P<0.001). In addition, lipohypertrophy was more common in patients experiencing hypoglycemia (61.5%; P<0.001) and those with unexplained hypoglycemia (75.5%, P<0.001).

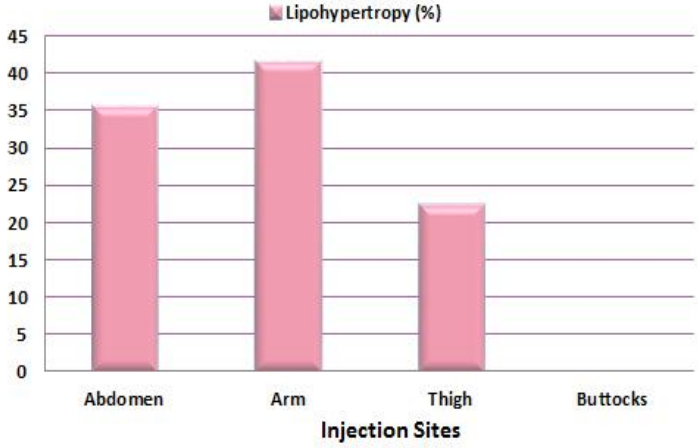

Figure 1: The prevalence of lipohypertrophy at injection sites

Table 2. Perceived obstacles of individuals with type 2 diabetes regarding not to do rotation, N=94

Variable	N (%)
Perceived obstacles regarding not to do rotation	
Development of pain or bleeding (Arm or leg)*	31 (27.0)
Abdominal lipoidosis	28 (24.0)
Fear (from injection)	3 (3.0)
Practical use (abdomen and arm)	23 (20.0)
Difficulty in injection (difficulty in getting undressed or grasping the needle)*	29 (25.1)
Larger abdomen	1 (0.9)

*Patients responded more than one

Table 3. Frequency of lipohypertrophy and according to relevant characteristics

Variable	Lipohypertrophy Not present (N=245)	Lipohypertrophy Present (N= 191)	P*
Gender			0.787
Female	157 (56.7)	120 (43.3)	
Male	88 (55.3)	71 (44.7)	
Age (year)			0.573
<50	25 (52.1)	23 (47.9)	
50-59	61 (55.0)	50 (45.0)	
60-69	99 (60.4)	65 (39.6)	
≥70	60 (56.2)	53 (43.8)	
Educational Status			0.082
Non-literate	17 (51.5)	16 (48.5)	
Primary school graduate	81 (54.0)	69 (46.0)	
Secondary school graduate	78 (66.1)	40 (33.9)	
High school or university graduate	69 (51.1)	66 (48.9)	
BMI kg/m^2			0.009
Normal weight	49 (66.2)	25 (33.8)	
Over weight	125 (59.5)	85 (40.5)	
Obese	71 (52.5)	81 (47.5)	
Training provider			<0.001
Nurse	177 (64.6)	97.(35.4)	
Doctor	41 (34.2)	79 (65.8)	
Chemist	27 (64.3)	15 (35.7)	
The duration of diabetes diagnosis			0.003
1-10 year	99 (66.0)	51 (34.0)	
≥10	146 (51.0	140 (49.0)	

Table 3. Frequency of lipohypertrophy and according to relevant characteristics (continued)

Variable	Lipohypertrophy Not Present (N=245)	Lipohypertrophy Present (N= 191)	P*
The duration of diabetes therapy (year)			0.063
≤2	49 (67.1)	24 (32.9)	
3-9	141 (56.0)	111 (44.0)	
≥10	55 (49.5)	56 (50.5)	
The number of daily injection			0.014
1	81 (63.3)	47 (36.7)	
2	87 (61.3)	55 (38.7)	
3	26 (47.3)	29 (52.7)	
4	51 (45.9)	60 (54.1)	
Needle length			
4 mm	70 (52.6)	63 (47.4)	<0.001
5 mm	104 (68.9)	47 (31.1)	
6 mm	58 (49.6)	59 (50:4)	
8 mm	13 (37.1)	22 (62.9)	
Injection site			<0.001
Single site (abdomen, arms or legs)	17 (19.3)	71 (80.7)	
Two sites (abdomen, arms or abdomen or legs)	83 (49.7)	84 (50.3)	
Three sites (abdomen, arms, legs or arm, leg and hip)	145 (80.1)	36 (19.9)	
>50 UI/day	89 (50.6)	87 (49.4)	
Types of insulin's			0.037
Only basal	87 (65.4)	46 (34.6)	
Basal + Bolus	65 (52.4)	59 (47.6)	
Pre-mixed insulin	93 (52.0)	86 (48.0)	
Between sites rotation			<0.001
Performing Systematic rotation	196 (63.9)	81 (36.1)	
Not performing Systematic rotation	49 (51.8)	110 (48.2)	
Intra-sites rotation (at least 1 cm distance between injections)			<0.001
Yes	199 (68.4)	92 (31.6)	
No	46 (31.7)	99 (63.5)	
The frequency of needle change			0.014
At each injection	101 (70.8)	57 (29.2)	
Not at each injection (at least 3-time use)	144 (30.8)	134 (69.2)	
Hypoglycemia			<0.001
Yes	74 (38.5)	118 (61.5)	
No	171 (70.1)	73 (29.9)	
Unexplained recurrent hypoglycemia			<0.001
Yes	26 (24.5)	80 (75.5)	
No	219 (64.4)	111 (33.6)	
Hb A1C			<0.001
<7	61 (93.8)	4 (6.2)	
7-7.9	46 (86.8)	7 (13.2)	
8- 8.9	71 (68.3)	33 (31.7)	
≥9	67 (31.3)	147 (68.7)	

*Chi-square test, p<0.05 considered as significant, **Defining patients using different sites daily or 2-5 days or administering each injection to different sites.

Discussion

The study aimed to investigate the frequency of lipohypertrophy, one of the most common complications of insulin therapy, and the factors affecting the development of lipohypertrophy.

In this study, the prevalence of lipohypertrophy in patients with type 2 diabetes was found to be 43.8%. The prevalence of lipohypertrophy in this study was found to be similar to those in the literature.[1,12] In a previous study conducted in the Aegean region of Turkey, the prevalence of lipohipertrophy was reported to be 48.8%.[3] It was determined that the frequency of lipohypertrophy has decreased in Turkey over a 10-years period. It is thought that this decrease results from the patients' preference for shorter needles (4 and 5 mm) for insulin administration.

In this study, it was determined that the frequency of lipohypertrophy was higher in patients who failed to alternate the injection site (systematic rotation) (48.0%) and those who did not perform intra-site rotation (63.5%). Similarly, in the literature, not performing site rotation in patients with diabetes was found to be an effective independent risk factor in the development of lipohypertrophy.[1-3,6,12] In a study conducted by Blanco et al., it was emphasized that the application of the proper site rotation is very effective for the prevention of lipohypertrophy.[2] Similarly, in this study, the incidence of lipohypertrophy (80.7%) was higher in patients who "only used one region" as the site of insulin

administration. In this study, however, as the number of sites used for insulin administration increased the incidence of lipohypertrophy decreased. In the literature, the most common reasons why individuals with diabetes do not alternate the site of insulin injection were decreased pain sensation in lipohypertrophic region[2,6] and practical and easy administration of the drug to the injection site.[6] In this study, pain or bleeding in the legs or arm (27%) gripping challenges in the arm (25.1%) and difficulty in clawing the outfits off (25.1%) were found to be the most common reasons why individuals with diabetes do not make rotation.

The incidence of lipohypertrophy was highest in arms (41.7%), followed by abdomen (35.7%). Lipohypertrophy in individuals with diabetes was found to be more frequent in abdominal region in studies conducted in European Union countries.[2,13,14] In a study conducted in Egypt, it was determined that lipohypertrophy mostly occurs in arms with the ratio of 55.0%.[15] The reason why individuals with diabetes in our country mostly prefer arm and abdomen for insulin injection is probably due to the practicality in stripping clothes as stated by the 20.0% of the patients. Twenty-four percent of individuals with diabetes prefer arms for injection because they think that insulin causes fat deposition in the abdominal region.

The frequency of lipohypertrophy was higher in patients who reused the needle tip at least three times (69.2%). Similar to the findings of this study, it was emphasized in the literature that reuse of needle tip is an important independent factor in the development of lipohypertrophy.[3,6] Puder et al., reported that repeated reuse of needle causes pain and bruising / bleeding in individuals with diabetes because of the deterioration of the silicone structure of the needle.[16] It was found in another study that reuse of needle causes much more pain and bacterial contamination and the local inflammatory changes in the injection site.[17] All individuals with type 2 diabetes participating in this study used insulin pen. Therefore, higher incidence of lipohypertrophy in our study may be due to the tissue trauma at the injection site caused by the deterioration of the silicone structure of the needle in patients using needle tip at least three times.

Lipohipthophy is more frequent in patients who administer insulin injections four times per day. The studies conducted in the literature and the results of this study also emphasize that the incidence of lipohypertrophy increases in parallel with the increase in the number of injections per day.[2,12]

Insulin itself shows a strong growth hormone effect.[2,9] In the study carried out by Blanco and colleagues, the incidence of lipohypertrophy was found to be less in patients receiving only basal insulin therapy than those receiving basal + bolus insulin therapy.[2] It is thought that as the number of daily injections administered to the injection site increases, the frequency of lipohipertrophy in the injection site increase because the region is exposed to much more insulin and thus trauma. Another finding of this study, namely lipohiptrophy is less frequent in patients who only administer basal insulin, supports this assertion. Because the patients who only use basal insulin inject once a day but those who receive basal + bolus therapy administer four or more injections per day.

In this study, lipohypertrophy was less frequent in individuals with diabetes using 5mm needle. It was also observed that the incidence of lipohypertrophy also increases with the length of needle. It was determined that needle length is an important independent factor affecting lipohypertrophy development and that lipohypertrophy was 7.41-fold more common in patients using 12 mm needles than those using 8 mm.[1] It was reported in clinical trials that 4mm needles are equally effective and safe with longer needles (5 mm and 8 mm).[11] It was reported in clinical guidelines of Tandon et al., that 4 mm needle provides better glycemic control and reduces the risk of intramuscular injection and thus less pain during the injection.[11]

In this study, the frequency of lipohypertrophy in patients diagnosed with diabetes ≥ 10 years was higher than those having shorter duration of diabetes diagnosis. Similar results were obtained in studies conducted in the literature.[1,12,15,18] It was reported in the literature that individuals with type 2 diabetes start to receive insulin therapy 10 years after diabetes diagnosis.[19] In this context, it can be concluded that insulin injection management of individuals with diabetes over 10 years is not good.

The frequency of lipohypertrophy is higher in patients with hypoglycemia and unexplained hypoglycemia. The findings of this study were found to be similar to those in the literature.[2,6] Blanco et al., emphasized that lipohypertrophy is a major contributor to the development of adverse clinical events and this contribution is not considered when patients experience these adverse clinical events. In addition, once again we observed in this study that HbA1C, an important clinical finding for individuals with diabetes, adversely affects lipohypertrophy.[2] The frequency of lipohypertrophy was found to be higher in patients with A1C level ≥9. Similarly, lipohypertrophy was more common in patients with elevated A1C levels (>7).[1,5,6,20] It was observed in the case study of Malwa et al., that pre-education A1C level of the patients receiving "injection site rotation education" was 10.0% and this level decreased to 7.8% after 3 months and thus the daily insulin requirement.[19] In this study, it is thought that A1C level was higher because individuals with diabetes did not alternate injection site at the recommended frequency.

The frequency of lipohypertrophy was higher in obese patients. Similar results were obtained in the literature. The patients with BMI of 25 or higher were found to have higher incidence of lipohypertrophy.[6,20] Our findings suggest that the amount of subcutaneous adipose tissue may play an important role in the development of lipohypertrophy.

Lipohypertrophy was more common in patients who received insulin injection education from the physician. In a study conducted by Li and colleagues, the incidence of lipohypertrophy in the tertiary hospitals was found to be significantly lower than that in the second and primary care hospitals.[12] This finding can be attributed to the larger number of certified diabetes nurses employed

in the tertiary care hospitals.[12] In the clinical guideline, the lack of educated diabetes trainers is considered as one of the barriers to insulin therapy in patients with diabetes.[11]

In Turkey, diabetes nurses cannot provide diabetes education without diabetes certificate. They receive this certificate if they are successful in the exam after one month of serious theoretical and practical education. However, physicians and pharmacists do not receive a specific education regarding insulin administration and are not subjected to any examination. Because the physicians and pharmacists do not have full-time, insulin injection-specific duty, higher incidence of lipohypertrophy is an expected result.

Conclusion

In conclusion, healthcare worker who provides insulin education, the duration of diabetes, the number of injections administered daily, needle length, the number of injection sites used, insulin types, site rotation, intra-site rotation and needle changing frequency were determined as the important risk factors affecting the development of lipohypertrophy. In addition, it was also determined that the incidence of lipohypertrophy was higher in patients with hypoglycemia and lipohypertrophy and those with high BMI and A1C levels. Diabetes educators should necessarily examine insulin injection site in insulin administration education provide education to the patients about the factors affecting the development of lipohypertrophy (site rotation, needle re-use, etc.). It is recommended that diabetes educations should be provided by the full-time diabetes nurses with special certification in this field. There are only case studies on lipohypertrophy management in the literature. Therefore, randomized controlled interventional studies for the prevention of lipohypertrophy development are needed.

Two certified diabetes nurses worked for the detection of lipohypertrophy. The level and actual frequency of lipohypertrophy could be determined using an ultrasonic device but not because the device was too expensive and research did not receive any funding.

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Ethical issues

None to be declared.

Conflict of interest

The authors declare no conflict of interest in this study.

References

1. Al Ajlouni M, Abujbara M, Batieha A, Ajlouni K. Prevalence of lipohypertrophy and associated risk factors in insulin-treated patients with type 2 diabetes mellitus. Int J Endocrinol Metab 2015; 13 (2): e20776. doi: 10.581 2/ijem.20776.
2. Blanco M, Hernandez MT, Strauss KW, Amaya M. Prevalence and risk factors of lipohypertrophy in insulin-injecting patients with diabetes. Diabetes Metab 2013; 39 (5): 445-53. doi:10.1016/j.diabet.2013.05.006.
3. Vardar B, Kızılcı S. Incidence of lipohypertrophy in diabetic patients and a study of influencing factors. Diabetes Res Clin Pract 2007; 77 (2): 231-6. doi: 10. 1016/j.diabres.2006.12.023.
4. Ji J, Lou Q. Insulin pen injection technique survey in patients with type 2 diabetes in Mainland China in 2010. Curr Med Res Opin 2014; 30 (6): 1087-93. doi: 10.11 85/03007995.2014.895711.
5. Szpowska A, Skorka A, Pankowska E. Lipoatrophy associated with rapid-acting Insulin analogues in young patients with type 1 diabetes mellitus. Pediatr Endocrinol Diabetes Metab 2008; 14 (2): 117-8.
6. Al Hayek AA, Robert AA, Braham RB, Al Dawish MA. Frequency of lipohypertrophy and associated risk factors in young patients with type 1 diabetes: a cross-sectional study. Diabetes Ther 2016; 7 (2): 259-67. doi: 10.1007 /s1 3 3 00-016-0161-3.
7. Dar IH, Dar SH, Wani S. Insulin lipohypertrophy: a non-fatal dermatological complication of diabetes mellitus reflecting poor glycemic control. Saudi Journal of Medicine & Medical Sciences 2013; 1 (2): 106-8. doi: 10.4103/1658-631X.123646.
8. Johansson UB, Amsberg S, Hannerz L, Wredling R, Adamson U, Arnqvist HJ, et al. Impaired absorption of insulin aspart from lipohypertrophic injection sites. Diabetes Care 2005; 28 (8): 2025–7.
9. Richardson T, Kerr D. Skin related complications of insulin therapy: Epidemiology and emerging management strategies. Am J Clin Dermatol 2003; 4 (10): 661-7.
10. Erdfelder E, Faul F, Buchner A. GPower: a general power analysis program. Behav Res Methods Instrum Comput 1996; 28 (1): 1–11.
11. Tandon N, Kalra S, Balhara YPS, Baruah MP, Chadha M, Chandalia HB, et al. Forum for injection technique (FIT), India: the Indian recommendations 2.0, for best practice in insulin injection technique, 2015. Indian J Endocrinol Metab 2015; 19 (3): 317-31. doi: 10.4103/2230-8210 .15 2762.
12. Li FF, Fu SM, Liu ZP, Liu XR, Hu CJ, Li QF. Injection sites lipohypertrophy among 736 patients with type 2 diabetes of different-grade hospitals. Int J Clin Exp Med 2016; 9 (7): 13178-83.
13. De Coninck C, Frid A, Gaspar R, Hicks D, Hirsch L, Kreugel G, et al. Results and analysis of the 2008-2009 insulin injection technique questionnaire survey. J Diabetes 2010; 2 (3):168-79. doi: 10.1111/j.1753-0407 .20 10.00 077.x.
14. Hernar I, Haltbakk J, Broström A. Differences in depression, treatment satisfaction and injection behavior in adults with type 1 diabetes and different degrees of lipohypertrophy. J Clin Nurs 2017; 26 (23-24): 4583-96. doi: 10.1111/jocn.13801.
15. Omar MA, El-Kafoury AA, El-Araby RI. Lipohypertrophy in children and adolescents with type 1 diabetes and the associated factors. BMC Res Notes 2011; 4 (1): 290. doi: 10.1186/1756-0500-4-290.
16. Puder JJ, Atar M, Muller B, Pavan M, Keller U. Using insulin pen needles up to five times does not affect needle tip shape nor increase pain intensity. Diabetes Res Clin

Pract 2005; 67 (2): 119-23. doi:10.1016/j.diabres. 2004. 0 6.001.
17. Misnikova IV, Dreval AV, Gubkina VA, Rusanova EV. The risks of repeated use of insulin pen needles in patients with diabetes mellitus. Journal of Diabetology 2011; 2 (1): 2.
18. Cunningham MT, McKenna M. Lipohypertrophy in insulin-treated diabetes: prevalence and associated risk factors. J Diabetes Nurs 2013; 17 (9): 340–3.
19. Mlawa G, Balami D, Deshmukh S, Croft M, Bodmer C, Patel M. Insulin-induced lipohypertrophy, past, present and future-are we losing the battle? Endocrine Abstracts 2010; 22: 173.
20. Ji L, Sun Z, Li Q, Qin G, Wei Z, Liu J, et al. Lipohypertrophy in China: prevalence, risk factors, insulin consumption, and clinical impact. Diabetes Technol Ther 2017; 19 (1): 61-7. doi: 10.1089/dia.2016.0334.