

## Lipohypertrophy among Insulin-Treated Patients

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**Objective:** To evaluate insulin injection practice, prevalence and risk factors of lipohypertrophy (LH) among insulin-treated patients.

**Design:** A Retrospective Study.

**Setting:** Two Primary Health Centers, Bahrain.

**Method:** Ninety-five insulin-treated patients were included in the study from 3 January 2016 to 31 May 2016. The following data were documented: age, sex, educational level, type of diabetes, duration of diabetes, duration of insulin treatment, number of injections, type of insulin, daily insulin dose, needle size, site of injection, frequency of needle change, frequency of injection site rotation and frequency of checking the injection site. Diabetes control and Body Mass Index (BMI) were documented. Ultrasound examination of the injection site was performed.

**Result:** Ninety-five insulin-treated patients were included in the study. Thirty-five (36.8%) patients had LH. Seventy-two (75.8%) patients were obese females with poorly controlled type 2 diabetes. Forty-seven (49.5%) patients were using insulin for less than five years. Ninety-three (97.8%) patients were using  $\leq 6$  mm needle; 85 (89.5%) were using the needle once at a time and were doing daily rotation. The injection site was never checked in all except one (1.1%) patient. There was a highly significant statistical association between LH and level of education, the number of injections and the site of injection. Mean subcutaneous fat thickness were 12.3 mm (arm), 17.8 mm (thigh) and 23.3 mm (abdomen).

**Conclusion:** Lipohypertrophy is prevalent among our patients and could be related to improper insulin injection technique and lack of regular check of the injection sites. Therefore, patients and health providers' education is necessary to reduce its prevalence.

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Diabetes mellitus (DM) is becoming a global epidemic. Type 2 DM is the most common type of diabetes. Several studies found that, with time, most patients would eventually need insulin therapy as a treatment to control their blood sugar<sup>1,2</sup>. Early intervention is essential to control hyperglycemia and prevent or delay microvascular or macrovascular complications; insulin stands in the forefront in diabetes management<sup>3-5</sup>.

The use of insulin is not without risk. Beside hypoglycemia and weight gain, it could lead to various skin complications. LH is the most common skin-related insulin complication<sup>6</sup>. LH is defined as a visible or palpable lesion felt as a rubbery or thickened area when palpated<sup>7</sup>.

Patients' education regarding the correct injection technique, detection and management of LH is important for several reasons. LH is common among insulin-treated patients as found in many studies<sup>6,8-10</sup>. The factors leading to LH are preventable<sup>6,8-10</sup>. LH could lead to poor metabolic control, decreased insulin absorption and unexplained hypoglycemia.

Education could lead to lower incidence of LH, improve metabolic control, decrease hypoglycemic attacks, lower daily insulin doses and cost<sup>6,8,11-13</sup>.

In Bahrain, a recent study revealed that approximately 85% of the patients were on insulin therapy<sup>14</sup>. Despite that, there are no studies regarding insulin injection techniques, LH or associated risk factors.

The aim of this study is to evaluate insulin injection techniques, prevalence and risk factors of LH among insulin-treated patients attending primary care diabetic clinics.

### METHOD

Insulin-treated patients attending diabetes clinics were included in the study. The centers were chosen randomly, and the study was conducted from 3 January 2016 to 31 May 2016. Patients who were on insulin for less than six months were excluded.

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Lipohypertrophy was checked by the clinic nurse. US study of the patients' injection sites was performed and was read and reported by one radiologist. Body Mass Index (BMI) and glycated hemoglobin (A1C) were recorded.

Data was analyzed using SPSS version 22. Chi-squared test was used to assess the association between LH and other factors. Multiple logistic regression models that included all the studied risk factors and LH as the dependent variable were set to determine the independent predictors for LH.

## RESULT

Ninety-five patients were reviewed. Their clinical and personal characteristics are shown in table 1.

**Table 1: Clinical and Personal Characteristics of the Patients**

Characteristics	Number (%)
<b>Gender</b>	
Males	23 (24.2%)
Females	72 (75.8%)
<b>Total</b>	<b>95 (100%)</b>
<b>Age Group</b>	
< 40	7 (7.4%)
40 to < 50	9 (9.5%)
50 to < 60	26 (27.4%)
60 to < 70	35 (36.8%)
≥70	18 (18.9%)
<b>Total</b>	<b>95 (100%)</b>
<b>Educational Level</b>	
Illiterate	22 (23.2%)
Primary	11 (11.6%)
Intermediate	14 (14.7%)
Secondary	36 (37.9%)
University	12 (12.6%)
<b>Total</b>	<b>95 (100%)</b>
<b>Body Mass Index (kg/m<sup>2</sup>)</b>	
< 18	1 (1.1%)
18 to < 25	7 (7.4%)
25 to < 30	22 (23.1%)
≥ 30	63 (66.3%)
Missing Data	2 (2.1%)
<b>Total</b>	<b>95 (100%)</b>
<b>Type of Diabetes</b>	
1	3 (3.2%)
2	92 (96.8%)
<b>Total</b>	<b>95 (100%)</b>
<b>Duration of Diabetes (years)</b>	
< 5	4 (4.2%)
5 to 10	7 (7.4%)
10 to 15	26 (27.4%)
15 to < 20	20 (21%)
≥ 20	35 (36.8%)
Missing Data	3 (3.2%)
<b>Total</b>	<b>95 (100%)</b>
<b>Glycated Hemoglobin (mmol/mol)</b>	
< 53	27 (28.4%)
53 to < 64	18 (19%)
64 to < 75	15 (15.8%)
75 to < 86	10 (10.5%)
≥ 86	19 (20%)
Missing Data	6 (6.3%)
<b>Total</b>	<b>95 (100%)</b>

The table shows that half of the patients were elderly and two-thirds were females with long-standing poorly controlled type 2 diabetes.

Tables 2 and 3 show the duration and type of insulin, dose, type, duration and injection technique.

**Table 2: Insulin Treatment of the Patients**

Characteristics	Number (%)
<b>Duration of Insulin Treatment (years)</b>	
6 months to < 1 year	8 (8.4%)
1 to < 5	39 (41.1%)
5 to < 10	19 (20%)
10 to < 15	12 (12.6%)
15 to < 20	8 (8.4%)
≥ 20	7 (7.4%)
Missing Data	2 (2.1%)
<b>Total</b>	<b>95 (100%)</b>
<b>Type of Insulin Used</b>	
Analog	92 (96.8%)
Human	3 (3.2%)
<b>Total</b>	<b>95 (100%)</b>
<b>Number of Daily Injections</b>	
1	11 (11.6%)
2	31 (32.6%)
3	21 (22.1%)
4	31 (32.6%)
> 4	1 (1.1%)
<b>Total</b>	<b>95 (100%)</b>
<b>Average Insulin Dose (units/day)</b>	
< 30	11 (11.6%)
30 to 60	37 (38.9%)
60 to 100	26 (27.4%)
> 100	21 (22.1%)
<b>Total</b>	<b>95 (100%)</b>

**Table 3: Injection Technique**

Characteristics	Number (%)
<b>Needle Size (mm)</b>	
4	2 (2.1%)
5	41 (43.1%)
6	50 (52.6%)
8	1 (1.1%)
> 8	1 (1.1%)
<b>Total</b>	<b>95 (100%)</b>
<b>Frequency of Needle Change</b>	
At every injection	85 (89.5%)
Every 2 to 3 injections	9 (9.4%)
Every 4 to 5 injections	1 (1.1%)
After more than 5 injections	0 (0%)
<b>Total</b>	<b>95 (100%)</b>
<b>Site of Injection*</b>	
Arm	58
Abdomen	59
Thigh	64
Others	3
<b>Frequency of Injection Site Rotation</b>	
At every injection	85 (89.5%)
Every week	6 (6.3%)
Occasionally (when remembered)	0 (0%)
Use one site only	4 (4.2%)
<b>Total</b>	<b>95 (100%)</b>
<b>Frequency of Checking the Injection Site</b>	
Not at all	94 (98.9%)
Once a year	1 (1.1%)
Every visit	0 (0%)
When there is a problem	0 (0%)
<b>Total</b>	<b>95 (100%)</b>

\* patients used more than one injection site

Forty-seven (49.5%) patients were using insulin for less than five years; the majority were using insulin analogs; approximately one-third of the patients were using four injections daily.

Ninety-one (95.7%) patients were using either 5 mm or 6 mm size needles; 85 (89.5%) patients were using the needle once at a time and were doing daily site rotation. The injection sites were never checked, except in one (1.1%) patient.

We found a highly significant statistical association between LH and the following risk factors: educational level, number of injections and injections in the arm and abdomen. There was no significant association with other risk factors, see table 4.

**Table 4: Presence or Absence of LH and Risk Factors**

Risk Factor	P-value
Gender	0.055
Level of Education	0.015
Age Group	0.594
Type of Diabetes	0.887
Duration of Diabetes	0.839
Duration of Insulin Treatment	0.056
Number of Injections	0.018
Insulin Dose	0.687
Needle Size	0.096
Site of Injection (Arm)	0.044
Site of Injection (Abdomen)	0.001
Site of Injection (Thigh)	0.836
Frequency of Needle Change	0.198
Site Rotation	0.210
Checking the Injection Site	0.192
Control of Diabetes	0.368
BMI	0.530

LH was present in 35 (36.8%) patients. Skin and subcutaneous (SC) thicknesses of the examined patients are shown in table 5.

**Table 5: US Findings of the Examined Patients**

Examined Site	Minimum (mm)	Maximum (mm)	Mean (mm)
Skin Thickness (Arm)	1.75	4.60	2.86
Skin Thickness (Thigh)	1.00	11.0	3.22
Skin Thickness (Abdomen)	1.75	4.20	3.10
Subcutaneous Thickness (Arm)	3.55	29.3	12.3
Subcutaneous Thickness (Thigh)	6.95	35.0	17.8
Subcutaneous Thickness (Abdomen)	5.95	44.8	23.3

There was no statistically significant association between age, sex and thicknesses (skin and SC) ( $P>0.05$ ). However, there was a strong correlation between BMI and arm and thigh SC (but not skin) thickness ( $P=0.005$  and  $0.008$ ; respectively). There was no statistically significant association between BMI and abdominal SC thickness ( $P=0.154$ ).

**DISCUSSION**

In our study, LH was present in 36.8% of the patients. The majority was using 5 mm or 6 mm size needles, approximately

90% were using the needle once at a time and were practicing daily rotation. There was a statistically significant association between the presence of LH and educational level, the number of injections and injection in the arm and abdomen.

The prevalence in this study is similar to a study by Al Ajlouni et al<sup>9</sup>. However, other studies found significantly higher prevalence while others found lower prevalence<sup>8,15-18</sup>. In our study, 36.8% prevalence is considered high because approximately 50% were recent insulin users, all (except one) were using small needles (less than 8 mm) and approximately 90% were using the needle once at a time. Longer insulin duration, longer needles and needle reuse was consistently found to be associated with LH<sup>8-10,16,18</sup>.

Adherence to proper injection techniques impacts glycemic control and could decrease the prevalence of LH significantly<sup>8,11,13</sup>. Improper insulin injection practice could explain the high prevalence of LH and poor glycemic control in our patients.

The guidelines recommend regular inspection of injection site at each visit or at least annually to detect and avoid areas with LH<sup>7,19,20</sup>. Unfortunately, we found that injection sites were never inspected in all (except one) patients. Furthermore, it is also recommended that patients follow the weekly rotation of the injection after dividing the sites into quadrants (for abdomen) or halves (for thighs)<sup>7,19</sup>. Only 6 (6.3%) patients were using this procedure. In addition, the upper arm is not currently recommended because of difficulty in accessing the correct zone for injection and the SC fat thickness is small compared to other recommended sites, which increases the risk of intramuscular injection leading to erratic insulin absorption and hypoglycemia<sup>7</sup>.

Patients with higher educational level were less likely to have LH which is consistent with other studies<sup>10,18</sup>. Injection in the abdomen was significantly less likely to develop LH ( $P$ -value 0.001), which is similar to the findings of another study<sup>18</sup>. Recent guidelines emphasize the use of abdomen especially in lean subjects because of the large injection zone and thick SC fat<sup>7,19</sup>.

While needle size and needle reuse were found to be strongly associated with LH among several studies, in our study we found insignificant association<sup>8-10,21</sup>. The likely explanation is that most of our patients use small needles ( $\leq 6$  mm) and do not reuse the needle. Reuse is a common practice worldwide driven mainly by cost. The majority of Indian ( $>90\%$ ) patients use the needle 3-5 times before discarding it<sup>22</sup>.

Site rotation was not found to be associated with LH compared to other studies. Blanco et al found that only 5% of their patients who rotated correctly had LH. On the other hand, 98% of those with LH either did not rotate or practice wrong site rotation<sup>8</sup>. That may explain the high LH prevalence in our study. Only six (6.3%) patients were practicing site rotation as recommended by the guidelines<sup>7</sup>.

Examining the injection site is important as not all LH could be visible and need to be palpated to be detected<sup>6,7</sup>. In addition, detection of LH would give the opportunity to educate the patient to avoid injection in LH areas which could lead to poor glycemic control and unexplained hypoglycemia<sup>6,8,11,12</sup>. It was found that when patients received injection training from a diabetes nurse, they had a significant decrease in A1C, unexpected hypoglycemia and glucose variability<sup>23</sup>.

US of our patients revealed higher mean skin thickness compared to recent studies<sup>24,25</sup>. The mean skin thickness found was less than 2.5 mm compared to 3.1 mm in our study. Racial differences may explain these findings<sup>24</sup>. The US findings indicate the risk for intramuscular injections in the arm if using  $\geq 6$  mm sized needle, but the risk is almost nonexistent in the abdomen and the thigh.

Using a 4 mm needle should be recommended in patients who prefer to use the arm. The use of 8 mm needle should be avoided because of the risk for IM injections<sup>7,26</sup>. Approximately 90% of our patients were obese and had thicker SC fat. We found a significant association between SC thickness of the arm and thigh and BMI, which is consistent with recent studies<sup>24,25</sup>. Therefore, the results could not be extrapolated to patients with normal BMI where the risk for IM injection could be higher.

## CONCLUSION

**Lipohypertrophy was prevalent among our patients and could be related to improper insulin injection practice and absence of regular check of the injection sites. Patients and healthcare providers' education is necessary to reduce the prevalence of LH.**

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**Competing Interest:** None.

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