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Original Research Article

PREVALENCE AND RISK FACTORS FOR LIPOHYPERTROPHY IN INSULIN-INJECTING PATIENTS WITH TYPE 2 DIABETES MELLITUS

Rahul Valisetty[1], Eshwar Dasari[2], Ketavath Sravyasree[3]

[1]*Assistant Professor, Department of General Medicine, Government Medical College and Hospital, Nalgonda, Telangana, India.*
[2]*Assistant Professor, Department of General Medicine, Government Medical College and Hospital, Nalgonda, Telangana, India.*
[3]*Assistant Professor, Department of General Medicine, Government Medical College and Hospital, Nalgonda, Telangana, India.*

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Corresponding Author:
Dr. Rahul Valisetty,
Assistant Professor, Department of General Medicine, Government Medical College and Hospital, Nalgonda, Telangana, India.
Email: rahulvalisetty@gmail.com

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ABSTRACT

Background: Lipohypertrophy (LH) frequently occurs in people with type 2 diabetes mellitus (T2DM) treated with insulin, which may negatively affect insulin absorption and glycemic control. This study aimed to identify the prevalence of LH and its associated risk factors among patients with T2DM who inject insulin.

Materials and Methods: This cross-sectional observational study included a sample of 40 patients with T2DM who were undergoing insulin therapy. Demographic and clinical parameters, methods of insulin administration, and glycemic control data were obtained. LH was evaluated through physical assessment. Relevant statistical tests and multivariate logistic regression analyses were used to analyze the associations.

Results: LH was prevalent in 60. LH was found to be closely related to increased duration of diabetes ($p<0.001$), insulin therapy for > 5 years (OR=6.85, p=0.001), needle reuse > 5 times (OR=5.92, p=0.003), irregular rotation of sites (OR=4.37, p=0.01), and longer needles (OR=3.95, p=0.02). HbA1c (9.4+1.5% vs 8.1+1.2%, p=0.003), insulin doses, and hypoglycemic episodes were also increased in

Conclusion: LH is common in T2DM patients who inject insulin and have poor injection technique, along with poor glycemic outcomes. Regular education on insulin administration to lower LH levels and achieve better metabolic control should be conducted.

Keywords: Lipohypertrophy, Prevalence, Type 2 Diabetes Mellitus, Insulin injection.

INTRODUCTION

Diabetes Mellitus type 2 (T2DM) is a global health challenge with an estimated number of about 537 million adults have it across the world, and this number is projected to reach 643 million by 2030.[1] Many patients with T2DM will ultimately have to be treated with insulin because their β-cells are progressively dysfunctional and unable to control their glycemic levels with the means of oral antidiabetic drugs only.[2] The most effective treatment in this regard is subcutaneous insulin injection which provides good glycemic control. However various complications accompany insulin therapy whereby the most common and, in most cases, unnoticed complication is the lipohypertrophy (LH). Lipohypertrophy refers to the thickening of subcutaneous fat tissue at the site of repeated insulin injections. It is characterized by painless swellings under the skin and it is related to diminished insulin absorption, enhanced fluctuations in glycemia, and unexplained bouts of hypoglycemia (3, 4). In diabetic patients who are on insulin treatment, the prevalence of LH varies between 20 to over 60 percent according to the studies done and it depends on the education provided to the patient, the duration he or she had been given insulin, and compliance with the proper method of insulin injection.[5,6] Repeated injection on the same anatomical site and failure to rotate the location of the site of injection are considered to be major causes of LH development.[7] In addition, longer periods of insulin therapy, high body mass

index (BMI), uncontrolled glycemic levels and inadequate diabetes education appear to be related to an augmented risk of LH.[8,9] Reuse of needles, which is widely experienced in regions with low resources, is a risk factor not only with regards to LH occurrence but also contributes to the deformation of the needle tips, which further worsens the trauma to the local tissues.[10] Lipohypertrophy has serious clinical implications. Injection of insulin into LH sites tends to be absorbed in an unpredictable manner causing blood glucose level fluctuations and unstable insulin dynamics.[11] This leads to inadequate glycemic control and can raise the demands of increased insulin doses, leading to high treatment expenses and patient burden. Additionally, LH has psychological social contexts that influence compliance with treatment because of beauty issues and unease.[12] LH is relevant clinically but it has been underdiagnosed many times because healthcare professionals fail to inspect injection sites regularly. Evidence-based observations have demonstrated the effective reduction of the occurrence and severity of LH through frequent check-ups and palpation of the sites of injection combined with well-organized instructions on the appropriate injection habits.[13] Therefore, estimating the prevalence and treatable risk factors of LH in insulin-treated individuals with T2DM is critical for the development of preventive measures and positive outcomes for patients. The current study aimed to evaluate the prevalence of lipohypertrophy among patients with type 2 diabetes mellitus receiving insulin therapy and to analyze associated risk factors associated with the development of LH.

MATERIALS AND METHODS

This was a cross-sectional observational study conducted over a period of six months in the outpatient department of General Medicine, Government Medical College and Hospital, Nalgonda, Telangana. Institutional ethical approval was obtained for the study after duly following ethical protocol for human research based on the Helsinki Declaration. Written consent was obtained from all the participants of the study after explaining the nature of the study in vernacular language.

Inclusion Criteria

1. Diagnosed cases of type 2 diabetes mellitus.
2. Adult males and females
3. On insulin therapy (any regimen) for ≥6 months.
4. Willing to participate and provide informed consent.

Exclusion Criteria

1. Patients with type 1 diabetes mellitus.
2. Patients on insulin pump therapy.
3. Presence of generalized lipodystrophy or skin diseases at injection sites.
4. Critically ill or mentally unfit to participate.

A total of 40 adult patients with diagnosed type 2 diabetes mellitus, who had been receiving subcutaneous insulin therapy for a minimum duration of 6 months, were enrolled consecutively after obtaining written informed consent. The data collection was done by interviewing each participant using a pre-validated structured questionnaire to collect the following data. Demographic details (age, gender, duration of diabetes), Clinical history including duration and dose of insulin therapy, Type and frequency of insulin injections, Needle length, gauge, and reuse practices, Site rotation habits and insulin storage practices, Hypoglycemic episodes in the past 3 months.

A detailed clinical examination of all common insulin injection sites (abdomen, thighs, arms, buttocks) was performed. Lipohypertrophy was identified through inspection and palpation by a trained physician using standardized criteria:

1. Palpable thickening or rubbery areas under the skin.
2. Loss of normal subcutaneous texture or visual swelling.
3. Absence of pain on palpation.

Biochemical Parameters investigated in the cases were the most recent HbA1c values (within the last 3 months), fasting blood glucose, and body mass index (BMI) were recorded.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using SPSS version 25.0 in Windows format. Continuous variables were expressed as mean, standard deviation, frequencies, and percentages. The prevalence of lipohypertrophy was calculated as a proportion. Associations between lipohypertrophy and risk factors were assessed using a chi-square test test for categorical variables, and a Student's t-test for continuous variables. A p-value <0.05 was considered statistically significant.

RESULTS

In this study a total of 40 cases receiving insulin therapy were included out of these we found the prevalence of lipohypertrophy (LH) in (24/40) 60% of cases. The mean age of the population was comparable in both LH positive and LH negative groups the overall mean age was 58.4 ± 9.2 years given in Table 1. The analysis of the table also showed that patients with LH had significantly longer diabetes duration (14.8 ± 4.9 years vs. 9.3 ± 4.1 years) and the p-value was (< 0.001). Similarly, longer insulin use duration (6.7 ± 2.4 years vs. 3.1 ± 1.5 years) and the p-value was (< 0.001) compared to those without LH. The BMI was slightly higher in the LH group (29.1 ± 3.6 vs. 27.3 ± 3.9 kg/m²), this difference was not statistically significant (p = 0.11). These findings suggest that the long duration of diabetes and insulin use are major contributors to the development of lipohypertrophy.

Table 1: Prevalence and Demographic Characteristics

Characteristic	Overall (n=40)	LH (positive) (n=24)	LH (Negative) (n=16)	p-value
Lipohypertrophy Prevalence		24 (60%)		
Age (years)	58.4 ± 9.2	59.8 ± 8.5	56.3 ± 10.1	0.22
Gender (Male: Female)	22:18	12:12	10:6	0.42
Diabetes Duration (yrs)	12.6 ± 5.3	14.8 ± 4.9	9.3 ± 4.1	<0.001*
Insulin Duration (yrs)	5.2 ± 2.8	6.7 ± 2.4	3.1 ± 1.5	<0.001*
BMI (kg/m^2)	28.4 ± 3.8	29.1 ± 3.6	27.3 ± 3.9	0.11

***Significant**

Table 2 shows the most important insulin injection practices and the association of these habits with LH. A strong correlation existed between needle reuse and LH-positivity. 62.5% of LH-positive patients re-used needles 6 or more times as compared to 6.3% of the LH-negative group ($p < 0.001$) with a relative risk (RR) of 9.38 (95% CI: 3.1028.4). Similarly, the irregular site rotation was also much more frequent within the LH group (79.2% vs. 25.0%; $p = 0.001$). The length of the needle also demonstrated a difference, with LH being more prevalent among those using 8 - 12 mm length of needles (75.0%) than those using 4 - 6 mm (25.0 %) ($p = 0.007$). Statistical significance of the frequency of injection was not reached. This shows that poor injection technique is a major modifiable risk factor for LH.

Table 2: Insulin Therapy Practices

Practice	LH (positive) (n=24)	LH (Negative) (n=16)	p-value	RR (95% CI)
Needle Reuse				
Never	2 (8.3%)	10 (62.5%)	<0001*	-
1-5 times	7 (29.2%)	5 (31.3%)	0.89	1.75 (0.65-469)
Times	15 (62.5%)	1 (6.3%)	<0001*	9.38 (3.10-28.4)
Site Rotation				
Regular	5 (208%)	12 (75.0%)	0.001*	-
Irregular	19 (79.2%)	4 (25.0%)	0.001*	3.17 (1.67-6.00)
Needle Length				
4-6 mm	6 (25.0%)	11 (68.8%)	0.007*	-
8-12 mm	18 (75.0%)	5 (31.3%)	0.007*	2.64 (1.35-5.15)
Injection Frequency				
1-2/day	8 (33.3%)	9 (56.3%)	0.15	-
≥ 3/day	16 (66.7%)	7 (43.8%)	0.15	-

***Significant**

Table 3 shows the glycemic control indicators between LH-positive and LH-negative patients of the study. Those with LH had significantly poorer glycemic control, with higher HbA1c (9.4 ± 1.5% vs. 8.1 ± 1.2%) and the p values were ($p = 0.003$) and fasting blood glucose levels (178 ± 42 mg/dL vs. 142 ± 36 mg/dL) and the p values were ($p = 0.005$). They also required higher insulin doses (0.78 ± 0.22 IU/kg/day vs. 0.62 ± 0.18) and $p = 0.01$ and experienced more frequent hypoglycemic episodes (5.2 ± 2.1 vs. 2.4 ± 1.8; $p < 0.001$). These findings show the clinical relevance of LH as a contributor to erratic glucose control and increased insulin requirements.

Table 3: Glycemic Control Parameters

Parameter	LH (positive) (n=24)	LH (Negative) (n=16)	p	Mean Difference
HbA1c (%)	9.4± 1.5	8.1 ± 1.2	0.003*	+1.3
Fasting BG (mg/dL)	178±42	142 ± 36	0.005*	+36
Insulin Dose (IU/kg/day)	0.78 ± 0.22	0..22 ± 0.18	0.01*	+0.16
Hypoglycemia Episodes (Brno)	5.2±2.1	2.4± 1.8	<0.001*	+2.8

***Significant**

In Table 4, the anatomical distribution of the lipohypertrophy is represented. The abdomen was the most commonly involved site, LH in 83.3%, and it was the most frequently exclusively involved site as well (50.0%). The second most affected part was the thighs (62.5%), the arms (37.5%) and the buttocks (29.2%). These trends show that the abdomen is the most preferred site for insulin injection and hence failure to rotate the site may result in tissue change due to chronic injury. It was also interesting to note that there were no incidents that reported the buttocks as the most prone area indicating that it would have been less used as a point of insulin injection.

Table 4: Site-Specific Prevalence of Lipohypertrophy

Injection Site	LH Prevalence	Most Affected Site
Abdo men	20 (83.3%)	12 (50.0%)
Thighs	15 (62.5%)	8 (33.3%)
Arms	9 (37.5%)	4 (16.7%)
Buttocks	7 (29.2%)	0 (0%)

Table 5 shows the comparison of the distribution of insulin regimens between LH-positive and LH-negative patients. Premixed insulin was the most commonly used regimen overall and significantly more frequent in the LH group (58.3% vs. 25.0%) and (p = 0.04). Basal-bolus therapy was evenly distributed between both groups (p = 0.57), while basal-only therapy was more frequent in the LH-negative group (50.0% vs. 8.3%) and (p = 0.003). These findings may show that regimens requiring more frequent injections, such as premixed insulin, may predispose patients to LH due to repetitive use of limited anatomical sites.

Table 5: Insulin Regimen Distribution

Regimen	Overall (n=40)	LH (positive) (n=24)	LH (Negative) (n=16)	P value
Premixed	18 (45.0%)	14 (58.3%)	4 (25.0%)	0.04*
Basal-Bolus	12 (30.0%)	8 (33.3%)	4 (25.0%)	57
Basal only	10 (25.0%)	2 (8.3%)	8 (50.0%)	0.003*

***Significant**

Table 6 depicts the results from multivariate logistic regression identifying independent predictors of lipohypertrophy. Insulin use for more than 5 years (OR = 6.85, p = 0.001), needle reuse beyond 5 times (OR = 5.92, p = 0.003), irregular site rotation (OR = 4.37, p = 0.01), and use of longer needles (>8 mm) (OR = 3.95, p = 0.02) were all significant predictors. While premixed insulin showed a trend (OR = 3.10), it did not reach statistical significance (p = 0.07). These results reaffirm the importance of education on injection techniques and site rotation to minimize LH risk.

Table 6: Multivariate Predictors of Lipohypertrophy

Risk Factor	Adjusted OR	95%CI	p-value
Insulin duration > 5 years	6.85	2.14 – 21.93	0.001
Needle Reuse > 5 years	5.92	1.87 – 18.71	0.003
Irregular site rotation	4.37	1.39 – 13.72	0.01
Needle length > 8mm	3.95	1.25 – 12.45	0.02
Premixed insulin	3.10	0.92 – 10.42	0.07

DISCUSSION

The current study reveals that there is a high prevalence (60%) of lipohypertrophy (LH) in patients with type 2 diabetes mellitus (T2DM), who inject insulin. Other similar studies conducted internationally have found the prevalence rates of LH ranging from 28% to 64%.[3,13] These findings divulge that LH remains a prevalent and often overlooked complication of subcutaneous insulin therapy. There was a significantly higher occurrence of LH in patients with chronic usage of insulin which appears to be one of the major contributing factors.[11,14] The present study showed that insulin administration practices are strongly linked to LH development. The most important among them appears to be needle reuse and irregular site rotation which were commonly prevalent in cases of LH. The results of this study showed that patients who reused needles more than five times had a nearly tenfold increased risk of LH which was in agreement with other similar studies where they identified needle reuse as the important risk factor for tissue trauma and inadequate insulin absorption.[5,13] In the same way, patients who failed to rotate injection sites regularly had having three times greater likelihood of development of LH. Studies in this field have emphasized the importance of site rotation to prevent lipodystrophy.[14] We also found that the impact of needle length on development. Patients using longer needles (8-12mm) had having significantly higher risk of developing LH compared to those who used shorter-length needles (4-6mm). It appears the longer needles increase the risk of injecting into muscle tissue or cause subcutaneous trauma both of which may contribute to LH formation.[15] These results show that the use of shorter needles is safer and equally effective in most patients. Such recommendations have already been issued by the Forum for Injection Technique (FIT) guidelines.[16] The results of the study showed that glycaemic control was significantly poor in patients with LH. This was evidenced by the higher HbA1c levels, fasting glucose, and daily insulin doses. This shows that LH tends to impair insulin absorption leading to erratic glycemic control and increased insulin requirements.[7] Moreover, the LH-positive group showed more frequent hypoglycemic episodes due to inconsistent insulin absorption from altered subcutaneous tissues.[4] In terms of anatomical distribution, the abdomen was the commonest affected region followed by thighs and arms. Such a pattern is a reflection of common injection practice, including the fact that patients may choose some of the accessible sites over others, which results in overuse and subsequent hypertrophy.[17] The absence of the involvement of other sites in 50% of the LH-LH-positive cases points out the pressing importance of organized education on injection technique. The multivariate analysis showed that the duration of insulin therapy, reuse of needles, haphazard rotation of sites, and having a long needle all acted

independently to predict LH. Whereas a premixed insulin regimen tended to increase LH risk, it was not statistically significant. Yet, the premixed regimens are more likely to have a more frequent injection, which can be more dangerous in case people do not work on keeping their technique stable.[18] Overall, our study underlines the urgent need for continuous patient education on injection techniques, including site rotation, needle disposal, and appropriate needle length selection. Regular clinical examination of the injection site and the use of shorter needles can substantially reduce the burden of LH development and improve glycemic control for patients.

CONCLUSION

In conclusion, the prevalence of lipohypertrophy among patients with type 2 diabetes mellitus treated with insulin was very high. Factors such as poor injection practices, such as needle reuse, inconsistent site rotation, and the use of longer needles, were important risk factors. In addition, lipohypertrophy is associated with poor glycemic control and more episodes of hypoglycemia. These findings highlight the need for regular inspection of injection points and teaching patients the proper methods of insulin administration to reduce complications and enhance therapeutic success.

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