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ORIGINAL ARTICLE

Lipohypertrophy in insulin injecting patients with diabetes mellitus: an under-recognized barrier for glycemic control

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Abstract

Background Lipohypertrophy is the one of the commonest local complications that significantly affects glycemic control in patients of diabetes mellitus on treatment with insulin. Our study aimed at assessing the clinical and ultrasonographic characteristics and risk factors for lipohypertrophy on the abdomen in a cohort of insulin-injecting Indian diabetes patients.

Materials Eighty-eight consecutive patients with type 1 (15/88) or type 2 diabetes mellitus (73/88) were included in this cross-sectional study conducted over a period of 6 months. The prevalence of lipohypertrophy and associated risk factors was assessed by clinical examination. A novel ultrasonographic characterisation of lipohypertrophy (LH) using a predetermined grading system was performed by two sonologists who were blinded to the underlying clinical findings. Kappa statistics was used to calculate the agreement between the clinical and ultrasound methods of detection of lipohypertrophy.

Results The prevalence of lipohypertrophy was 68% on clinical examination and 90% on ultrasonography with moderate kappa agreement (60%). The commonest patterns on clinical and ultrasonographic assessment were Grade 2 (palpable and visible − 43%) and nodular hyperechoic subcutaneous dystrophy (33%), respectively. Duration of insulin use, incorrect site rotation, and repeated needle reuse ($p < 0.01$) were the most important risk factors. The total daily dose of insulin ($p = 0.01$) and mean Hba1c ($p = 0.02$) were significantly higher in those with clinically detected lipohypertrophy. The needle length, caliber, the mode of delivery, or regimen of insulin used did not significantly impact development of lipohypertrophy ($p = 0.15$).

Conclusion A thorough clinical examination of insulin injection sites is of paramount importance in detecting lipohyperyrophy. Adequate control of risk factors can significantly impact insulin requirements and glycemic control, while ultrasonography can prove to be a novel and sensitive tool to detect abdominal lipohypertrophy in the majority of patients, even when clinical examination is non-contributory.

Keywords Lipohyeprtrophy · Insulin · Injection · Rotation · Diabetes

Introduction

Intensive insulin therapy is the corner stone of treatment to achieve optimal glycemic control and reduce the long-term complications in type 1 diabetes mellitus and long-standing type 2 diabetes mellitus [1, 2]. This form of therapy is associated with cutaneous complications like erythema, pruritus, induration, lipohypertrophy, and atypical cutaneous infections. Lipohypertrophy is one of the commonest local complications associated with subcutaneous insulin therapy and one of the important under-recognized causes for poor glycemic control [1]. Insulin lipohypertrophy denotes a benign abnormal accumulation of adipose tissue at the insulin injection site, with the lipogenic effect of insulin being postulated as one of the key mechanisms [3]. However, factors like repeated microtrauma from long-term injection use, reuse of blunted needles, and improper injection technique are suggested to have an equally important contribution to the development of lipohypertrophy. The prevalence of lipohypertrophy in

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insulin injecting patients with diabetes mellitus has ranged from 30 to 65 % in various studies [3–6].

Ultrasonographic screening of insulin injecting sites for lipohypertrophy has been shown to reveal a higher detection rate of 86.5% when compared with 30.7% by clinical examination in a study by Natalia et al. [7]. Ultrasonography may also help in the characterization of insulin lipohypertrophy.

However, there is limited literature on the prevalence of lipohypertrophy in Indian subjects [8, 9]. The data on the ultrasonographic characterization of these lesions and the risk factors are also limited. Therefore, we undertook this study to look at the prevalence of lipohypertrophy in insulin injecting patients with diabetes mellitus as detected by clinical examination and ultrasonography. We also studied their characteristics on ultrasonography, the risk factors, and their association with glycemic status.

Material and methods

This was a cross-sectional study where in consecutive patients with type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) on subcutaneous insulin injections attending the department of Endocrinology as an outpatient were recruited. Subjects using insulin pumps, pregnant women, those patients on immune-suppressive agents, and those with secondary diabetes such as acute and chronic pancreatitis, fibrocalcific pancreatic diabetes, pancreatic cancers, acromegaly, Cushing's syndrome, hyperthyroidism, primary hyperparathyroidism, primary hyperaldosteronism, drug-induced diabetes, congenital and acquired lipodystrophic diabetes, and syndromic presentations were excluded.

Data were obtained regarding the age, sex, body mass index (BMI), type of diabetes mellitus, time since diagnosis of DM, duration of insulin use, insulin regimen, insulin injecting devices, needle length, frequency of needle change, and rotation of insulin injecting site. All subjects underwent a detailed clinical examination including anthropometry. Hba1c measured by the high-performance liquid chromatography method (HPLC) within the past 3 months was taken for the analysis.

The presence of lipohypertrophy was assessed in patients by clinical examination of the abdomen by inspection and palpation and were graded from 0 to 2 as follows: grade 0: no changes, grade 1: visible hypertrophy of the fat tissue but palpably normal consistency, grade 2: massive thickening of the fat tissue with a higher consistency [10].

Though some studies have considered lipoatrophy as grade 3, the rarity of occurrence and completely different etiopathogenetic mechanisms leading to lipoatrophy make it a distinct entity [11]. Therefore, we have not considered it in our grading system for lipohypertrophy.

All subjects underwent an ultrasound screening of the dermis and subcutaneous tissue of the abdomen for evidence of lipohypertrophy by the radiologist who was blinded to the patient's clinical findings. Ultrasonography was performed using a Philips EPIQ 5G machine, transducer L18-5 broadband linear array working on 18 to 5 MHz extended operating frequency. On the ultrasonography, the normal dermis is homogenously hyperechoic when compared with the subdermal fatty tissue and ranges between 1 and 4 mm in thickness. There is a well-defined and regular demarcation between dermis and the subcutis [12]. The subcutaneous tissue offers a hypoechoic background secondary to the fat lobules and a hyperechoic connective web with very thin septa between the lobules. The hyperechoic muscularis fasciae are seen beneath the subcutis layer [9]. Based on the thickness, echogenity, echotexture, delineation between dermis, subcutis and muscularis layers, and subcutis vasculature on ultrasound, the lipohypertrophy was further classified based on the system suggested by Kapeluto and colleagues [12, 13].

Statistical analysis

A sample size of 80 subjects was required to study the prevalence of lipohypertrophy on clinical examination with a precision of 10% and 95% confidence interval based on the 30% prevalence of lipohypertrophy reported by Natalia et al. [7]. The clinical characteristics of the study populations were expressed as mean and standard deviation and percentages. The agreement between the clinical and ultrasonographic detection of the lipohypertrophy was determined using Kappa. The factors influencing the development of lipohypertrophy were evaluated using the chi-square test, and $p < 0.05$ was considered significant. Independent variables influencing the occurrence of lipohypertrophy were evaluated using multiple logistic regression analysis.

Results

A total of $n = 116$ consecutive patients with diabetes mellitus ($n = 89$ T2DM and $n = 27$ T1DM subjects) on insulin therapy were screened for the study, of which $n = 88$ (64 male, 24 female) were studied based on predetermined inclusion criteria and willingness to give informed consent. The study duration was for a period of one year (March 2016 to February 2017). The T2DM patients constituted 83% ($n = 73$) of subjects and 17% ($n = 15$) were T1DM. The baseline characteristics of the T1DM and T2DM subjects are provided in Table 1. The mean duration of insulin usage was 77.5 ± 79.4 months. The total daily dose (TDD) of insulin was 55.3 ± 28.0 units. The mean Hba1c of the study subjects was 8.9 ± 2.1%. Sixty patients (68.2%) were found to have the clinical evidence of lipohypertrophy, of which 22 (36.7%) patients were

Table 1 Baseline characteristics in the study population (n = 88)

Characteristics (N = 88)	Type 1 (n = 15)	Type 2 (n = 73)
Age (years)	25.2 ± 7.2	56.7 ± 10.3
BMI (kg/m)2	21.2 ± 4.3	27.5 ± 4.6
Duration of DM (years)	16.2 ± 7.8	22.9 ± 9.9
Insulin use (months)	100.6 ± 84.0	73.7 ± 78.6
Total insulin dose (IU/day)	44.40 ± 16.52	57.58 ± 40.80
HbA1c (%)	7.99 ± 3.0	9.08 ± 1.85

found to have grade 1 and 38 (63.3%) patients were found to have grade 2 lipohypertrophy, based on the clinical classification of insulin lipohypertrophy [10].

On ultrasound screening of insulin injecting sites at abdomen, 79 (89.7%) patients were found to have evidence of lipohypertrophy. Based on ultrasonographic characteristics, lipohypertrophy was further classified as in Fig. 1.

On comparison of the clinical and ultrasound screening for lipohypertrophy, the ultrasonography detected an additional 19 patients with lipohypertrophy who were not detected clinically. There was a moderate agreement (kappa value 0.545) between the clinical and ultrasound detection of lipohypertrophy (Table 2).

Factors associated with development of Lipohypertrophy

The comparison of the various clinical characteristics of patients with the clinical evidence of lipohypertrophy versus those without lipohypertrophy is shown in Table 3.

Table 2 Comparison between clinical and ultrasound detection of lipohypertrophy (n = 88)

Method of detection*	Lipohypertrophy status (n = 88)	
	Present	Absent
Clinical (%)	60 (68.2%)	28 (31.8%)
Ultrasound (%)	79 (89.8%)	9 (10.2%)

*Degree of agreement between clinical and USG method: Kappa value = 0.545

Lipohypertrophy was significantly more common in the T2DM when compared with the T1DM (p = 0.05). The clinical evidence of lipohypertrophy was significantly higher in men, obese subjects, those not rotating insulin injecting sites, and frequency of needle reuse > 5 and > 60 months of insulin use (Table 4). The total daily dose of insulin was significantly higher in patients with clinical evidence of lipohypertrophy as compared with those without lipohypertrophy (61.60 ± 23.13 v 41.89 ± 17.93, p = 0.01). Similarly, the mean Hba1c was significantly higher in those with clinical evidence of lipohypertrophy (9.52 ± 2.14 vs 8.46 ± 1.99, p = 0.02), with the significance persisting after dividing the study subjects based on Hba1c values of either less than or more than 7% . On multiple logistic regression, the duration of insulin use more than 60 months and incorrect insulin site rotation technique were associated with the risk of insulin lipohypertrophy (Table 4).

A sub-group analysis was performed to compare those detected with lipohypertrophy by USG (n = 79) with those having no ultrasound evidence of lipohypertrophy (n = 9). The mean Hba1c (9.12 ± 2.53 vs 8.68 ± 1.39 %, p = 0.03) and total

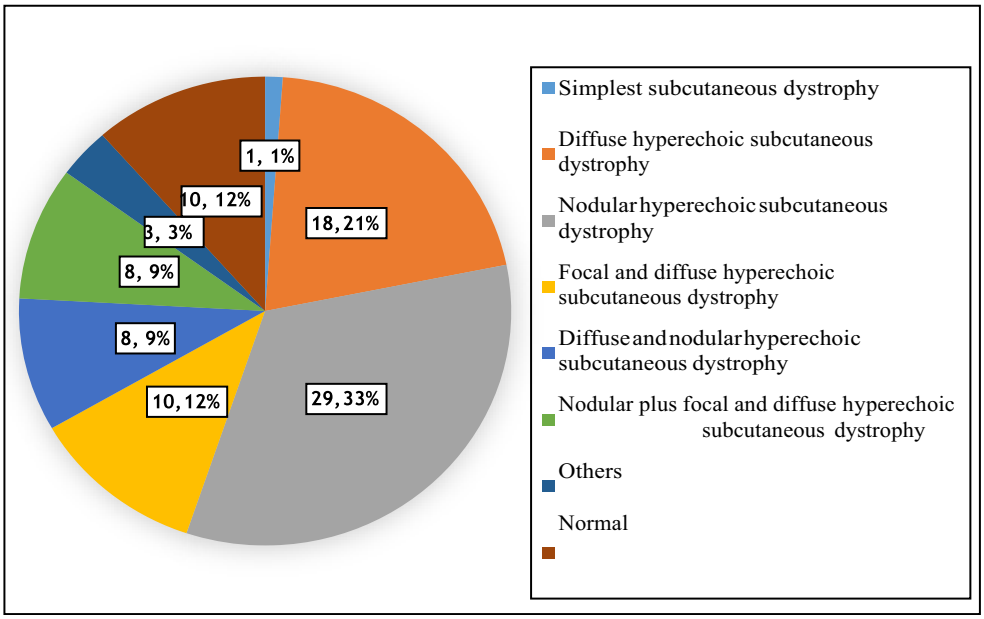

Fig. 1 Ultrasound classification of lipohypertrophy

Table 3 Comparison of characteristics of patients with lipohypertrophy ($n = 60$) and patients without lipohyperttrophy ($n = 28$) detected by the clinical method

Variable	Total subjects number (%) ($N = 88$)	Lipohypertrophy status by clinical method		*P* value (chi-square)
		Present ($N = 60$) Number (%)	Not present ($N = 28$) Number (%)	
Gender				
Men	64 (72.7%)	48 (75%)	16 (25%)	0.039
Women	24 (27.3%)	12 (50%)	12 (50%)	
BMI				
Obese	52 (60.5%)	39 (75%)	13 (25%)	0.041
Not obese	36 (39.5%)	21 (55%)	15 (45%)	
Type of diabetes				
Type 1 DM	15 (17%)	7 (46.7%)	8 (53.3%)	0.05
Type 2 DM	73 (83%)	53(72.7%)	20(27.3%)	
Change of injection site (rotation)				
Injection site not changed	77 (87.5%)	58 (75.3%)	19 (24.7%)	0.001
Injection site changed	11 (12.5%)	2 (18.2%)	9 (81.8%)	
Needle change frequency				
≤ 5 times	38 (43.7%)	22 (57.9%)	16 (42.1%)	0.042
> 5 times	49 (56.3%)	38 (77.6%)	11 (22.4%)	
Duration of insulin usage				
< 60 months	49(55.7%)	29 (59.2%)	20 (40.8%)	0.02
> 60 months	39 (44.3%)	31 (79.5%)	8 (20.5%)	
Insulin regimen				
Premix	54 (61.4%)	38 (70.4%)	16 (29.6%)	0.16
Basal bolus	21 (23.9%)	16 (76.2%)	5 (23.8%)	
Split mix	13 (14.8%)	6 (46.2%)	7 (53.8%)	
Use of device				
Syringe only	72 (81.8%)	51 (70.8%)	21 (29.2%)	0.50
Pen only	12 (13.6%)	7 (58.3%)	5 (41.7%)	
Syringe + Pen	4 (4.5%)	2 (50%)	2 (50%)	
Length of needle				
4 mm	12 (13.6%)	7 (58.3%)	5 (41.7%)	0.35
6 mm	66 (75.0%)	47(71.2%)	19(28.8%)	
8 mm	10 (11.4%)	6 (60%)	4 (40%)	
Needle calibration				
G– syringe	76 (86.4%)	53 (69.7%)	23 (30.3%)	0.33
G – pen (4mm)	11 (12.5%)	6 (54.5%)	5 (45.5 %)	
31 G – pen (6mm)	5 (5.7%)	3 (60%)	2 (40%)	
HbA1c levels				
Less than 7%	15 (19.3%)	10 (66.7%)	5 (33.3%)	0.035
More than 7%	73 (80.7%)	50 (67.6%)	23 (32.4%)	
HbA1c level (mean)	8.90 ± 2.10	9.52 ± 2.14	8.46 ± 1.99	0.020
Total Daily Dose of insulin (mean IU/day)	55.3 ± 28.0	61.60 ± 23.1	41.89 ± 17.93	0.010
Type of insulin injection				0.29
Conventional	55 (62.6%)	38 (69.1%)	17 (30.9%)	
Analogue	33 (37.4%)	22 (66.7%)	11 (33.3%)	

daily dose of insulin (58.82 ± 25.16 v 44.78 ± 23.45 IU/d, $p = 0.05$) in the former was significantly higher than the latter. Amongst the risk factors, USG evidence of lipohypertrophy was higher in those not rotating injection sites ($p = 0.07$) and using insulin for more than 60 months ($p = 0.08$), with a trend towards statistical significance. The other factors failed to show significant differences between the two sub-groups, probably owing to the small sample size.

Table 4 Multiple logistic regression analysis of factors determining the risk of insulin lipohypertrophy

Risk factors	OR	*P* value	95% CI
Duration of insulin use > 60 months	4.1	.022	1.2–14.2
Needle reuse > 5 times	1.4	.476	0.5–4.3
Incorrect insulin site rotation technique	11.8	.002	2.4–58.2

Discussion

Diabetes mellitus (DM) is a chronic disease with every patient of type 1 DM and a large number of type 2 DM patients requiring insulin for optimal glycemic control. The most common local complication seen in patients with DM on treatment with insulin is lipohypertrophy [9, 14, 15].

In our study the prevalence of lipohypertrophy at the insulin injecting site was 68.2%. This is similar to a study Blanco et al. which showed a prevalence of 64.4% [5], while being significantly higher than Frid et al. who observed self-reported lipohypertrophy in 29.0% of patients while 30.8% were detected by health care professionals (HCPs) [16, 17]. On the basis of clinical examination, we have further classified lipohypertrophy according to grade 0 through grade 2. Majority of patients had grade 2 lipohypertrophy which is a massive thickening of fat tissue with higher consistency (n = 38, 43.8%), followed by grade 1 in 22 patients (25%) which is defined as a visible hypertrophy of fat tissue but palpably normal consistency. In a study done in T2DM patients, 62.1% had grade 0, 27.4% had grade 1, 9.7% had grade 2, and 0.2% had lipoatrophy [3]. This difference in clinical grading could be explained by the differences in the observer's perception and the subjective variation in visual findings for grade 1 lesion and the paucity of studies that have utilized this grading system. Further, clinical grading used in our study does not incorporate the subset of insulin-injecting patients who develop palpable but not visible hardening of subcutaneous fat, thus underlying the need for future refinement of this clinical gradation. However, irrespective of the differences in distribution amongst the different grades, the clinical prevalence of lipohypertrophy remains a significant problem in all the studies done so far.

One of the novel features of our study is the ultrasonographic characterisation of the lipohypertrophy using a predetermined grading system [12]. While previous investigators have used high-frequency ultrasound to delineate skin and subcutaneous adipose tissue thickness in insulin-injecting diabetes patients [18], its use in classifying lipohypertrophy has not been widely studied. Ultrasonography detected lipohypertrophy at the insulin injecting sites in 90% of the subjects in our study, which is similar to the study performed by Natalia et al. where in 86.5% of the subjects had evidence of lipohypertrophy when assessed by ultrasonography [19].

On further characterisation of lipohypertrophy based on the ultrasonographic findings, we found that nodular hyperechoic subcutaneous dystrophy was the most common form (33%), followed by the diffuse hyperechoic subcutaneous dystrophy (20.5%), focal and diffuse hyperechoic subcutaneous dystrophy (11.4%), and diffuse and nodular hyperechoic dystrophy (9%). The combination of nodular plus focal and diffuse hyperechoic subcutaneous dystrophy (3.3%) and simplest subcutaneous dystrophy (1.1%) were the least common types. There was substantial agreement amongst the two independent sonologists (kappa value 0.83) involved in our study. The literature on USG characterization of insulin site lipohypertrophy in different ethnic groups is limited, and our study is the first such characterization in Asian Indian patients. However, use of ultrasound for classifying subcutaneous changes of lipohypertrophy can be user-dependent and subjective, thus necessitating the role for expert sonologists in understanding the true clinical significance of the ultrasonographic descriptions of lipohypertrophy (Fig. 2).

The prevalence of lipohypertrophy was higher on ultrasound screening when compared with clinical examination (90% vs 68%) in our study. There was a moderate agreement between the USG and clinical screening of abdominal insulin injecting sites in detecting lipohypertrophy. This suggests that even with meticulous clinical examination, up to 20% or more cases of lipohypertrophy may be missed. Given the significant impact of lipohyertrophy on overall glycemic control, ultrasound evaluation can prove to be a necessary modality in identifying these undetected cases. Though cost and availability issues with routine use of ultrasound in all patients of lipohypertrophy need to be addressed in future multicenter studies, our data strongly suggests that methodical ultrasound evaluation by trained radiologists can be the investigation of choice in suspected abdominal lipohypertrophy, especially in scenarios where there is a presence of multiple risk factors (needle re-use, poor site rotation, etc) but clinical examination is non-conformative. Further, the relationship of various types of lipohypertrophy with respect to glycemic control has not been established and will need a prospective follow-up study to look at the difference in behaviour of individual types of lipohypertrophy with respect to their glycemic variability and their reversibility with the change in insulin injection techniques.

The prevalence of lipohypertrophy on clinical examination was higher in T2DM when compared with T1DM (73.6% vs 46.7%) in our study. This is in contrast to previous studies like Blanco et al. [5]. The decreased prevalence of clinically detected lipohypertrophy in our patients of T1DM when compared with type 2 can be attributed to the fact that T1DM patients included in our study are generally patients who are on our regular follow-up and therefore have been sensitized to the appropriate insulin usage techniques through repeated focussed diabetes education. Further, when compared with the

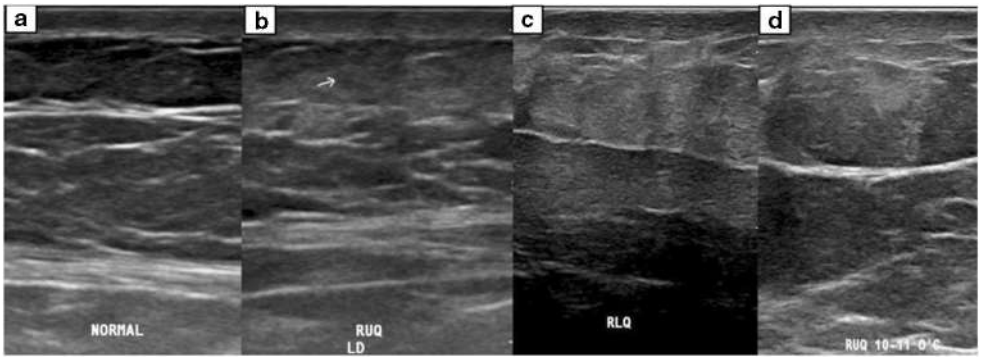

Fig. 2 Ultrasound images: (A) normal, (B) focal and diffuse hyperechoic subcutaneous dystrophy, (C) diffuse hyperechoic subcutaneous dystrophy, and (D) nodular hyperechoic subcutaneous dystrophy

previous studies, the number of T1DM patients in our study was much lower than the T2DM patients.

When we looked at the association of various factors with regard to the development of lipohypertrophy, the clinical evidence of lipohypertrophy was significantly higher in men, obese subjects, those not rotating insulin injecting sites, frequency of needle reuse on more than 5 occasions, and duration of insulin use of more than 60 months (all $p < 0.05$). The needle length, needle calibre, device used, regimen of insulin used, and type of insulin (conventional or analogue) had no influence on the development of lipohypertrophy. Similar findings on the risk factors of lipohypertrophy have been reported in a study by Bahar et al. [4].

The increase in the incidence of lipohypertrophy with the duration of insulin use has been described previously. In our study, the prevalence of lipohypertrophy was 59.1% (29/49) in those who were using insulin for less than 5 years as compared with 87.1% (27/31) in those who were using insulin for 5–10 years. Similar findings were reported previously [5] where the prevalence of lipohypertrophy was 48% in those using insulin for 1–5 years and progressively increased to 90% with increasing duration of insulin use beyond 20 years. Though predominantly attributed to the ability of injected insulin to act as a growth promoting factor for adipose tissue at the local insulin injection site, repeated trauma due to longer duration of injections per se can influence the formation of lipohyperttrophy. The higher prevalence of lipohypertrophy in type 2 diabetes and obese subjects, despite having a lower duration of insulin use than type 1 diabetes subjects, raises the intriguing possibility of insulin volume per injection playing a causative role. Since factors like diabetes education imparted to type 1 diabetes patients may have skewed the results, larger, prospective studies are needed to evaluate the pathological role of cumulative volume of insulin injected.

The prevalence of lipohypertrophy was also higher in those not rotating their injection sites correctly when compared with those who followed the correct rotation of insulin injecting sites which were similar to that reported in previous studies [5].

Another factor influencing the development of lipohypertrophy was the frequency of changing needles. Our study showed that the risk of developing lipohypertrophy increased with the re-use of the same needle more than 5 times (63%) when compared with those re-using needles less than 5 times (37%). In a study by Vardar et al [4], the prevalence of lipohypertrophy was 21% in those who changed their needle at every injection and this proportion increased to 51.2% and 75% in those who changed their needle at every 3rd and 5th injections respectively. The US FDA recommends injection needles for single use only, which may at times be impractical in countries like India, where socio-economic considerations need to be taken into account to arrive at more pragmatic solutions [19].

Amongst all the risk factors studied, the duration of insulin use of more than 60 months and the incorrect rotation of insulin injecting sites appeared to be the most important factors associated with the development of lipohypertrophy when assessed by multiple logistic regression in our study. Though frequency of needle re-use (> 5 times) led to nearly doubling of occurrence of lipohypertrophy (37% to 64%), it failed to show significant correlation on regression analysis. While this can be partly explained by the smaller sample size, it may also suggest that duration of insulin use and site rotation may be more important as contributory risk factors in our study. Overall, findings from correlation analysis point to the fact that issues pertaining to the technique of insulin injection are perhaps more important than the type of insulin being used for the development of lipohypertrophy. Different strategies have been employed worldwide to educate patients regarding insulin injection techniques, especially on injection site rotation and frequency of needle reuse. A prospective, randomized controlled trials to assess the impact of injection technique (IT) education, on insulin-treated patients with clinically observed LH over a period of 6 months, demonstrated a greater and faster improvement in the intervention arm [20]. In our institution, to teach our patients the correct technique of injection, we have included visual aids depicting the grid system of site rotation, which may have a better impact than verbal reinforcement and improve patients' adherence.

In our study, the patients with lipohypertrophy were 4 times more likely to have Hba1c more than 7%. Similar studies have shown that patients with Hba1c more than 7% were at least 3–5 times more likely to have lipohypertrophy [3], which

in turn led to a significantly higher total daily insulin dose requirement (56 IU/day vs 41 IU/day) [5].

At present there are worldwide 150–200 million insulin-using diabetes patients, of which approximately 3.2 million patients with diabetes in India are currently on insulin [21, 22]. This would contribute to a significantly increased financial burden of managing diabetes in India. Thus, a massive impact on healthcare expenditure can be achieved if development of lipohypertrophy in DM patients can be reduced by patient education on correct insulin injecting techniques. Comprehensive therapeutic education, preferably covering all topics related to insulin injection techniques, is one key area that is often overlooked in diabetes patients on insulin-injection therapy [23–25]. Innovative ways to involve the patient in the decision-making process through a discussion format of diabetes education has shown to be more effective than a rigid didactic form [26, 27]. Studies have shown better results with group education, while initiating the health-care provider in formal diabetes education training can ensure lower subsequent Hba1c values and better adherence [28]. Data from Indian studies (ITQ) show only 30% of Indian injectors get their sites checked this frequently with nearly a third only having sites check when they specifically complained and nearly 40% never having had their sites checked [8], while the worldwide data being even more dismal when compared with Indian studies in this regard [1]. This can be a major area of thrust in improving diabetes education in diabetes patients injecting insulin regularly.

Conclusion

Insulin lipohypertrophy is a common under-reported complication of insulin therapy leading to suboptimal glycemic control. While a thorough clinical examination of insulin injection sites has been traditionally used to detect lipohypertrophy, it may prove to be inadequate in more than one-fifth of cases. Our study provides evidence to suggest that systematic ultrasound evaluation may be successful in identifying majority of cases (> 90%) and larger studies identifying its role in standard diabetes care are necessary. Further, ultrasound-based characterization of abdominal lipohypertrophy lesions and its relation to glycemic variations and possible reversibility with correction of injection techniques are areas that need to be critically elucidated in future studies.

Improper insulin injecting technique is the most important risk factor for the development of lipohypertrophy. Increasing awareness about the lipohypertrophy and its risk factors amongst health care providers and educating the patients on correct insulin injection practices are key to solving the problem of insulin lipohypertrophy. The relatively better Hba1c in our type 1 diabetes subjects and lesser lipohypertrophy despite using multiple daily insulin injections for a longer duration emphasizes the beneficial effect of regular, patient-oriented diabetes education, both individually and in groups. For resource-limited countries like India, this can be a simple and cost-effective tool to mitigate lipohypertrophy in insulin-injecting diabetes patients. The strength of our study is the use of a novel ultrasonography-based gradation in addition to clinical examination for the detection of lipohypertrophy and study of various risk factors. The limitation of our study is that the impact of lipohypertrophy and its reversibility on the glycemic control could not be accurately assessed as it is a cross-sectional study and needs larger prospective studies.

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Compliance with ethical standards

The study was approved by the Institutional review board (IRB Min No 9926 dated 05.02.2016).

Conflict of interest The authors declare that they have no conflict of interest.

Informed consent Type 1 or type 2 DM subjects of age 18 years and older injecting insulin subcutaneously on the abdomen for at least 6 months duration were recruited after obtaining a written informed consent.

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