

Frequency and Associated Factors of Lipohypertrophy in Children and Adolescent with Type 1 Diabetes in a Single Tertiary Care Centre

Kashan Arshad¹, Aamir Naseem², Sommayya Aftab³, Syed Saddam Hussain⁴

- Fellow Pediatric Endocrinology and Diabetes, Department of Pediatric Endocrinology and Diabetes, Pediatric Unit-1, FMU/Allied Hospital, Faisalabad, Pakistan.*
Conceived the idea, Data collection, Literature search, Result processing, Writing manuscript
Fellow Pediatric Endocrinology and Diabetes, Department of Pediatric Endocrinology and Diabetes, University of Child Health Sciences, The Children's Hospital, Lahore, Pakistan.
Literature search, Result processing
Associate Professor of Pediatric Endocrinology and Diabetes, Department of Pediatric Endocrinology and Diabetes, University of Child Health Sciences, The Children's Hospital, Lahore, Pakistan.
Literature search, Writing manuscript
Fellow Pediatric Endocrinology and Diabetes, Department of Pediatric Endocrinology and Diabetes, University of Child Health Sciences, The Children's Hospital, Lahore, Pakistan.
Statistical analysis, Data collection

CORRESPONDING AUTHOR

Dr. Kashan Arshad
 Fellow Pediatric Endocrinology and Diabetes,
 Department of Pediatric Endocrinology and Diabetes,
 Pediatric Unit-1, FMU/Allied Hospital, Faisalabad,
 Pakistan.
 Email: kashan_arshad@hotmail.com

Submitted for Publication: 06-04-2024
 Accepted for Publication: 03-06-2024

How to Cite: Arshad K, Naseem A, Aftab S, Hussain SS. Frequency and Associated Factors of Lipohypertrophy in Children and Adolescent with Type 1 Diabetes in a Single Tertiary Care Centre. *APMC* 2024;18(2):137-140. DOI: 10.29054/APMC/2024.1593

ABSTRACT

Background: Type 1 diabetes mellitus (T1DM) is a disorder characterized by insulin insufficiency caused by the autoimmune destruction of pancreatic beta cells. Optimum control of T1DM needs insulin administration along with intensive education. Lipohypertrophy is one of the complications and risk factors of uncontrolled diabetes. **Objective:** To determine the frequency and associated factors of lipohypertrophy in children and adolescents with type 1 diabetes in a single tertiary care centre. **Study Design:** Cross-sectional descriptive study. **Settings:** Department of Pediatric Endocrinology and Diabetes, Pediatric Unit-1, FMU/Allied Hospital, Faisalabad, Pakistan. **Duration:** 6 months from January 2023 to June 2023. **Methods:** A total of 148 children and adolescents with type 1 diabetic patients were enrolled. All the children were examined for the presence of lipohypertrophy (LH), and different associated factors for lipohypertrophy were statistically assessed to determine its significance. **Results:** The mean age of children and adolescents with type 1 diabetes was 6.74 ± 2.67 years (3 to 12 years). Males and females were 85 (57.43%) and 63 (42.57%), respectively. The frequency of lipohypertrophy was found in 58/148 (39.19%) patients with male predominance (40/85). Failure to change the injection sites and the younger age group were the most important associated factors for lipohypertrophy. **Conclusion:** The frequency of lipohypertrophy (LH) is high among children and adolescents with T1DM. The most important associated factors for lipohypertrophy were the younger age group, failure to change the injection sites, syringe reuse, and poor diabetes control.

Keywords: Type 1 diabetes, Lipohypertrophy, Diabetes control.

INTRODUCTION

Type 1 Diabetes Mellitus (T1DM) is a disorder characterized by insulin insufficiency caused by autoimmune destruction of pancreatic beta cells.¹ T1DM is believed to affect 1.02 out of every 100,000 people in Pakistan.² Patients with T1DM are at significant risk of developing other autoimmune disorders with Hashimoto's thyroiditis (17-30%) and celiac disease (8%) being the most common.³ T1DM requires lifetime exogenous insulin administration, either as numerous daily injections (MDI) or via a continuous subcutaneous pump. In developing countries, MDI is commonly used by patients as a basal bolus or mixed/split regimen.⁴

It is observed that children with poorly controlled T1DM have a strong association with lipohypertrophy (LH)

(49.5%). In the presence of insulin, repeated damage to the same skin and subcutaneous tissue leads to LH over a certain period of time.⁵ Absorption of insulin injection into the lipohypertrophy area is very uncertain, leading to hypoglycemia and poor glycemic control.⁶ To prevent LH, it is critical to learn good injection technique and rotate the injection site on a regular basis, which will help in the appropriate delivery of insulin into the subcutaneous tissues, leading to good glycemic control.⁷

The development of LH may be affected by several factors, such as gender, the duration of insulin usage, injection site, failure to rotate injection sites, body mass index (BMI), and needle reuse.⁸

In Pakistan, children with T1DM often reuse the same needle or insulin syringe due to financial constraints,

leading to an increased risk of LH. However, there is very limited data available regarding it. Therefore, this study was planned to determine the frequency of lipohypertrophy in children and adolescents with T1DM in our population and to identify associated factors.

METHODS

This cross-sectional descriptive study was carried out for a period of 6 months at Department of Pediatric Endocrinology and Diabetes, Pediatric Unit-1, FMU/Allied Hospital, Faisalabad, Pakistan, after the approval of the ethical review committee vide letter no. 48-ERC/FMU/2022-23/307 dated: 23-01-2023. A total of 148 children and adolescents with T1DM aged 3–12 years were included in this study. The WHO sample size calculator was used to compute the sample size for a single proportion, with $P = 56.8\%$,⁹ confidence level = 95%, and margin of error = $d = 8\%$. The cases were chosen using a non-probability, consecutive sampling technique. Patients with a history of psychopathology, any concomitant chronic disease, and visual, hearing, or cognitive impairment were excluded.

Detailed characteristics such as age, gender, BMI, T1DM duration, insulin syringe reuse, and site rotation were noted. Obesity was defined by a BMI greater than the 95th centile for the corresponding age and gender. Insulin syringe reuse was defined as per EADSG guidelines,¹⁰ which reported use of a single syringe > 5 times as re-use of a syringe. The rotation of the site was deemed positive when the patient followed the sequence to rotate the site every day, i.e., left and right arm, left and right thigh, and abdominal area.

A fasting blood sample of the patients was sent for HbA1c levels, and a level of < 7% was taken as controlled diabetes and $\geq 7\%$ as uncontrolled diabetes. To confirm lipohypertrophy, all patients underwent a complete visual inspection and palpation procedure for the presence of a visible or palpable lump at the injection sites, as described by Gentile *et al.*¹¹

Data was collected on a specially constructed Performa and analyzed using SPSS version 25. Age, BMI, and duration of T1DM were provided quantitatively as mean and standard deviation. The qualitative data, including gender, diabetes control, syringe re-use, site rotation, obesity, and lipohypertrophy, were presented as frequencies and percentages.

The significance of the association of different factors such as gender, age groups, duration of T1DM, diabetes control, syringe reuse, and site rotation with LH was assessed. A chi-square test was used, with a P-value of 0.05 considered significant.

RESULTS

The mean age of children and adolescents with T1DM was 6.74 ± 2.67 years, with ages ranging from 3 to 7 years comprising 60.14% and 8 to 12 years comprising 39.86% of the cohort. Males and females were 85 (57.43%) and 63 (42.57%), respectively. The mean duration of T1DM was 3.86 ± 1.90 years, with less than ≤ 5 years (75%), and >5 years (25%). The mean body mass index was 23.43 ± 4.78 kg/m². The distribution of study subjects according to diabetes control, site rotation, syringe reuse, and presence of lipohypertrophy is shown in Table 1.

Table 1: Distribution of study subjects according to diabetes control, site rotation, syringe reuse and presence of Lipohypertrophy (n=148)

Number of Study Subjects			Percentage %
Diabetes Control	Yes	84	56.76%
	No	64	43.24%
Site Rotation	Yes	90	60.82%
	No	58	39.18%
Syringe Reuse	Yes	98	66.22%
	No	50	33.78%
Lipohypertrophy	Yes	58	39.19%
	No	90	60.81%

The frequency of lipohypertrophy was found in 58 cases (39.19%) of patients with male predominance (40/58) and a younger age group (8–12 years), as shown in Table 2.

Table 2: Stratification of Lipohypertrophy with respect to gender and age

Factors		Lipohypertrophy		P-value
		Yes	No	
Gender	Male	40	45	0.023
	Female	18	45	
Age (Years)	3-7	24	65	0.0001
	8-12	34	25	

Failure to change the injection sites, duration of DM, diabetes control, and syringe reuse were the significant associated factors for lipohypertrophy, as shown in Table 3.

Table 3: Stratification of Lipohypertrophy with respect to duration of DM, diabetes control, site of rotation, and syringe reuse

Associated factors		Lipohypertrophy		P-value
		Yes	No	
Site Rotation	Yes	26	64	0.0001
	No	32	26	
Duration of DM (Years)	≤ 5	38	73	0.032
	>5	20	17	
Diabetes Control	Yes	27	57	0.044
	No	31	33	
Syringe Reuse	Yes	44	54	0.046
	No	14	36	

DISCUSSION

By 2040, the estimated number of patients with T1DM will reach 642 million worldwide; previously, in 2019, the number of adults with diabetes was around 463 million.¹² To control the blood glucose level, T1DM patients need exogenous insulin injected subcutaneously, either as a basal bolus regime, a mixed/split regimen, or a continuous insulin infusion. The use of insulin is also needed in type 2 diabetic patients, who are difficult to control with oral hypoglycemic medicine alone.¹³

Lipohypertrophy (LH) is the most frequent cutaneous consequence of insulin therapy. Studies have shown that the occurrence of unexplained hypoglycemia is almost sixfold higher in patients with LH, and the occurrence of glycemic variability is about sevenfold higher.⁶ Patients with poor glycemic control have an increased chance of renal disease,¹⁴ ophthalmological complications,¹⁵ cardiovascular disease,¹⁶ and amputation.¹⁷ Furthermore, financial burden may also increase in T1DM patients with LH, as these patients use more insulin.¹⁸ During the routine checkup of T1DM patients, it is very important to differentiate LH from normal skin. In different studies, the frequency of LH in people with diabetes ranged from 1.9% to 73.4%.¹⁹

This study was conducted to determine the frequency and associated factors of lipohypertrophy in children and adolescents with type 1 diabetes in a single tertiary care Centre. In our cohort, the frequency of lipohypertrophy was found in 58 cases (39.19%). Similar clinical findings were found in studies done in Dublin (51%), Spain (64.4%), Alexandria (54.9%), and Pretoria (52%).¹¹ The very high incidence of LH was found in other studies, from 22 centers of seven European countries (27%).²⁰

According to a study by Al Hayek *et al.*, LH was distributed based on grade, with 47% being in grade 1, 33.7% being in grade 2, and 19.3% being in grade 3. In his study, 46% and 42.5% of patients failed to change the injection site and re-used needles, respectively.²¹ Other studies also reported that a strong correlation is present between the incidence of LH and the failure to change the injection sites. The correct rotation technique of insulin administration is very important to prevent the development of LH.²²

Tsadik AG *et al.* observed that 56.8% of his cohort had clinical lipohypertrophy. Factors that influence the occurrence of LH are the younger age group (65% in the 1- to 12-year-old age group), re-use of the insulin syringe (76.4%), and failure to change the injection site (65.6%). Patients using high doses of insulin (59.7%) and non-optimal glycemic control (89.3%) have a higher incidence of LH.⁹ During the insulin administration, it is quite common to re-use needles among patients with

T1DM.⁶ Due to repeated use, the needle gets deformed and is likely to raise the injection morbidity, and the patient is more likely to develop LH. The risk of infection is also very high due to the re-use of insulin needles. A study in Europe reported that the risk of LH was 31% higher in those patients who re-used needles.²³

A recent study reported that an increase in body mass index and repeated insulin injections into the same site were important associated factors for the development of LH.²⁴ Similar findings were found in our study where failure to change the injection site and syringe reuse were significant associated factors for lipohypertrophy.

CONCLUSION

The frequency of lipohypertrophy (LH) is higher among children and adolescents with T1DM. The most important associated factors for lipohypertrophy were a younger age group, failure to change the injection sites, syringe reuse, and poor diabetes control. This demonstrates the critical role of patient education in the prevention of LH, emphasizing the need to rotate injection sites correctly to avoid needle reuse and maintain diabetes control.

LIMITATIONS

The duration of the study was six months and could therefore only include a limited number of patients. A longer duration and across different hospitals in Punjab could provide a clearer picture of any underlying geographical distributions.

CONFLICT OF INTEREST / DISCLOSURE

No conflict of interest is involved.

ACKNOWLEDGEMENTS

None.

REFERENCES

1. Roep BO, Thomaidou S, van Tienhoven R, Zaldumbide A. Type 1 diabetes mellitus as a disease of the β -cell (do not blame the immune system?). *Nature Reviews Endocrinology*. 2021 Mar;17(3):150-61.
2. Ahmedani MY, Fawwad A, Shaheen F, Tahir B, Waris N, Basit A. Optimized health care for subjects with type 1 diabetes in a resource constraint society: A three-year follow-up study from Pakistan. *World journal of diabetes*. 2019 Mar 3;10(3):224.
3. Popoviciu MS, Kaka N, Sethi Y, Patel N, Chopra H, Cavalu S. Type 1 diabetes mellitus and autoimmune diseases: a critical review of the association and the application of personalized medicine. *Journal of Personalized Medicine*. 2023 Feb 26;13(3):422.
4. Janež A, Guja C, Mitrakou A, Lalic N, Tankova T, Czupryniak L, Tabák AG, Prazny M, Martinka E, Smircic-Duvnjak L. Insulin therapy in adults with type 1 diabetes mellitus: a narrative review. *Diabetes Therapy*. 2020 Feb; 11:387-409.
5. Elsayed S, Soliman AT, De Sanctis V, Fawzy D, Ahmed S, Alaaraj N. Insulin-induced lipodystrophy and predisposing factors in children and adolescents with type 1 diabetes mellitus (T1DM) in

- a tertiary care Egyptian center. *Acta Biomed.* 2023 Jun 14;94(3):e2023078.
6. Xu XH, Carvalho V, Wang XH, Qiu SH, Sun ZL. Lipohypertrophy: prevalence, clinical consequence, and pathogenesis. *Chinese Medical Journal.* 2021 Jan 5;134(01):47-9.
 7. Kalra S, Pathan F, Kshanti IA, Bay NQ, Nagase T, Oliveria T, Bajpai S. Optimising Insulin Injection Techniques to Improve Diabetes Outcomes. *Diabetes Therapy.* 2023 Nov;14(11):1785-99.
 8. Gunhan HG, Elbasan O, Imre E, Yavuz DG. Lipodystrophy Frequency according to Insulin Treatment Regimen in Type 2 Diabetic Patients: Is Insulin Injection Frequency Matters in Analog Insulin Era? *Acta Endocrinol (Buchar).* 2022 Apr-Jun;18(2):202-208.
 9. Tsadik AG, Atey TM, Nedi T, Fantahun B, Feyissa M. Effect of insulin-induced lipodystrophy on glycemic control among children and adolescents with diabetes in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. *Journal of Diabetes Research.* 2018 Jul 4;2018.
 10. Bahendeka S, Kaushik R, Swai AB, Otieno F, Bajaj S, Kalra S, et al. EADSG guidelines: insulin storage and optimisation of injection technique in diabetes management. *Diabetes Therapy.* 2019 Apr; 10:341-66.
 11. Gentile S, Guarino G, Giancaterini A, Guida P, Strollo F, AMD-OSDI Italian Injection Technique Study Group. A suitable palpation technique allows to identify skin lipohypertrophic lesions in insulin-treated people with diabetes. *Springerplus.* 2016 Dec; 5:1-7.
 12. Babakhanian M, Razavi A, Pordanjani SR, Hassanabadi S, Mohammadi G, Fattah A. High incidence of type 1 diabetes, type 2 diabetes and gestational diabetes in Central Iran: A six years results from Semnan health cohort. *Annals of Medicine and Surgery.* 2022 Oct 1;82.
 13. Bianchi C, Daniele G, Dardano A, Miccoli R, Del Prato S. Early combination therapy with oral glucose-lowering agents in type 2 diabetes. *Drugs.* 2017 Mar; 77:247-64.
 14. MacIsaac RJ, Jerums G, Ekinci EI. Effects of glycaemic management on diabetic kidney disease. *World journal of diabetes.* 2017 May 5;8(5):172.
 15. Mowatt L. Diabetic retinopathy and its risk factors at the University Hospital in Jamaica. *Middle East African Journal of Ophthalmology.* 2013 Oct 1;20(4):321-6.
 16. Smith KJ, Rabasa-Lhoret R, Strychar I, Karelis AD, Clyde M, Levasseur J, et al. Good vs. poor self-rated diabetes control: differences in cardiovascular risk and self-care activities. *Experimental and Clinical Endocrinology & Diabetes.* 2014 Mar 12:236-9.
 17. Noor S, Khan RU, Ahmad J. Understanding diabetic foot infection and its management. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews.* 2017 Apr 1;11(2):149-56.
 18. 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 Technology & Therapeutics.* 2017 Jan 1;19(1):61-7.
 19. Deng N, Zhang X, Zhao F, Wang Y, He H. Prevalence of lipohypertrophy in insulin-treated diabetes patients: a systematic review and meta-analysis. *Journal of diabetes investigation.* 2018 May;9(3):536-43.
 20. Strauss K, Gols HD, Hannel I, Partanen TM, Frid A. A pan-European epidemiologic study of insulin injection technique in patients with diabetes. *Practical Diabetes International.* 2002 Apr;19(3):71-6.
 21. 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 Therapy.* 2016 Jun; 7:259-67.
 22. Hirsch LJ, Strauss KW. The injection technique factor: what you don't know or teach can make a difference. *Clinical Diabetes.* 2019 Jul 1;37(3):227-33.
 23. Deeb A, Abdelrahman L, Tomy M, Suliman S, Akle M, Smith M, et al. Impact of insulin injection and infusion routines on lipohypertrophy and glycemic control in children and adults with diabetes. *Diabetes Therapy.* 2019 Feb; 10:259-67.
 24. AlJaber AN, Sales I, Almigbal TH, Wajid S, Batais MA. The prevalence of lipohypertrophy and its associated factors among Saudi patients with type 2 diabetes mellitus. *Journal of Taibah University Medical Sciences.* 2020 Jun 1;15(3):224-31.